STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 179919

TO: Alton Pryor **Location: REM 4A39/4C70** **Art Unit: 1616** **February 17, 2006** **Case Serial Number: 09/887832**	**From: P. Sheppard** **Location: Remsen Building** **Phone: (571) 272-2529** **sheppard@uspto.gov**

Search Notes

ACCESS DB # _____

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FEB 16 2006

Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: Alton Pryor Examiner #: 74458 Date: 2/16/06
Art Unit: 1616 Phone Number: 2-0621 Serial Number: 09/887,832
Location (Bldg/Room#): RBM4A39 (Mailbox #): 4B3 FL Results Format Preferred (circle): PAPER DISK
****

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: _____

Inventors (please provide full names): _____

_____

Earliest Priority Date: _____

Search Topic:
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only ***Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.***

Search claims 18, 21, 22

a) (treat? or prevent? or control?) (3a) multiple sclerosi
b) monoamine oxidase or reserpine
c) a (p) b

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=> d his ful

     (FILE 'HOME' ENTERED AT 14:35:55 ON 17 FEB 2006)

     FILE 'REGISTRY' ENTERED AT 14:36:00 ON 17 FEB 2006
L1           245 SEA ABB=ON  PLU=ON  MONOAMINE OXIDASE?/CN OR RESERPINE

     FILE 'HCAPLUS' ENTERED AT 14:43:09 ON 17 FEB 2006
L2         33179 SEA ABB=ON  PLU=ON  L1 OR MONOAMINE(W) OXIDASE OR RESERPINE
L3         14082 SEA ABB=ON  PLU=ON  ("MULTIPLE SCLEROSIS-ASSOCIATED RETROVIRUS"
                 /CV OR "MULTIPLE SCLEROSIS RETROVIRUS"/CV OR "MULTIPLE
                 SCLEROSIS-ASSOCIATED RETROVIRUS 1"/CV OR "MULTIPLE SCLEROSIS-AS
                 SOCIATED RETROVIRUS 2"/CV) OR MULTIPLE(W)SCLEROSIS
L5         16906 SEA ABB=ON  PLU=ON  ("MONOAMINE OXIDASE"/CV OR "OXIDASE,
                 MONOAMINE"/CV OR "POLYAMINE OXIDASE"/CV) OR OXIDASE(A)MONOAMINE
L6         37143 SEA ABB=ON  PLU=ON  L2 OR L5 OR MAO OR MAOA?
L7            42 SEA ABB=ON  PLU=ON  L3 AND L6
L8            19 SEA ABB=ON  PLU=ON  L7 AND PD=<JULY 17, 2001
L9             8 SEA ABB=ON  PLU=ON  L7 NOT (2006 OR 2005 OR 2004 OR 2003 OR
                 2002)/PY
L10           19 SEA ABB=ON  PLU=ON  L8 OR L9
                 D STAT QUE
                 D IBIB ABS HITSTR L10 1-19

     FILE 'REGISTRY' ENTERED AT 14:44:49 ON 17 FEB 2006
L11            1 SEA ABB=ON  PLU=ON  TELE-METHYLHISTAMINE/CN
L12         4834 SEA ABB=ON  PLU=ON  H2

     FILE 'HCAPLUS' ENTERED AT 14:46:30 ON 17 FEB 2006
L13          507 SEA ABB=ON  PLU=ON  L11 OR TELEMETHYLHISTAMINE OR TELE(W)METHYL
                 HISTAMINE
L14         2053 SEA ABB=ON  PLU=ON  (L12 OR H2)(L)AGONIST
L15           64 SEA ABB=ON  PLU=ON  L2 AND (L13 OR L14)
L16           60 SEA ABB=ON  PLU=ON  L15 AND PD=<JULY 17, 2001
L17           60 SEA ABB=ON  PLU=ON  L15 NOT (2006 OR 2005 OR 2004 OR 2003 OR
                 2002)/PY
L18           60 SEA ABB=ON  PLU=ON  L16 OR L17
L20            2 SEA ABB=ON  PLU=ON  L18 AND NEURO?(5A)METABOL?
L21           31 SEA ABB=ON  PLU=ON  L18 AND (?MEDIC? OR ?THERAP? OR ?DRUG? OR
                 ?PHARMA? OR TREAT? OR PREVENT? OR CONTROL?)
L22           32 SEA ABB=ON  PLU=ON  (L20 OR L21) NOT L10
L25           15 SEA ABB=ON  PLU=ON  L18 AND (NEURO? OR NERV?)
L26           40 SEA ABB=ON  PLU=ON  L22 OR L25
                 D STAT QUE L26
                 D IBIB ABS HITSTR L26 1-40


     FILE HOME

     FILE REGISTRY
     Property values tagged with IC are from the ZIC/VINITI data file
     provided by InfoChem.

     STRUCTURE FILE UPDATES:   15 FEB 2006  HIGHEST RN 874326-73-5
     DICTIONARY FILE UPDATES:  15 FEB 2006  HIGHEST RN 874326-73-5

     New CAS Information Use Policies, enter HELP USAGETERMS for details.

     TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006
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Please note that search-term pricing does apply when conducting SmartSELECT searches.

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*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*
****

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

FILE HCAPLUS

FILE COVERS 1907 - 17 Feb 2006 VOL 144 ISS 9
FILE LAST UPDATED: 16 Feb 2006 (20060216/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 14:43:09 ON 17 FEB 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 17 Feb 2006  VOL 144 ISS 9
FILE LAST UPDATED: 16 Feb 2006  (20060216/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

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L1          245 SEA FILE=REGISTRY ABB=ON  PLU=ON  MONOAMINE OXIDASE?/CN OR
                RESERPINE
L2        33179 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L1 OR MONOAMINE(W) OXIDASE OR
                RESERPINE
L3        14082 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("MULTIPLE SCLEROSIS-ASSOCIATE
                D RETROVIRUS"/CV OR "MULTIPLE SCLEROSIS RETROVIRUS"/CV OR
                "MULTIPLE SCLEROSIS-ASSOCIATED RETROVIRUS 1"/CV OR "MULTIPLE
                SCLEROSIS-ASSOCIATED RETROVIRUS 2"/CV) OR MULTIPLE(W)SCLEROSIS
L5        16906 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("MONOAMINE OXIDASE"/CV OR
                "OXIDASE, MONOAMINE"/CV OR "POLYAMINE OXIDASE"/CV) OR OXIDASE(A
                )MONOAMINE
L6        37143 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L2 OR L5 OR MAO OR MAOA?
L7           42 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 AND L6
L8           19 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7 AND PD=<JULY 17, 2001
L9            8 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7 NOT (2006 OR 2005 OR 2004
                OR 2003 OR 2002)/PY
L10          19 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L8 OR L9


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=> d ibib abs hitstr l10 1-19

L10  ANSWER 1 OF 19  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2001:284696  HCAPLUS
DOCUMENT NUMBER:          135:56220
TITLE:                    Combined treatment with corticosteroids and
                          moclobemide favors normalization of
                          hypothalamo-pituitary-adrenal axis dysregulation in
                          relapsing-remitting multiple
```

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1088550	A1	20010404	EP 2000-308442	20000927 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 782986	B2	20050915	AU 2000-61307	20000926
US 6417229	B1	20020709	US 2000-671435	20000927
ZA 2000005217	A	20020328	ZA 2000-5217	20000928
CA 2321593	AA	20010401	CA 2000-2321593	20000929 <--
JP 2001097854	A2	20010410	JP 2000-298071	20000929 <--

PRIORITY APPLN. INFO.: US 1999-157083P P 19991001
OTHER SOURCE(S): MARPAT 134:261267

AB A method is provided for using the title compds., pharmaceutically acceptable salts thereof, or pharmaceutical compns. thereof, in the treatment of a disease, condition or disorder of the peripheral or central nervous system, including but not limited to Alzheimer's disease, stroke/cerebral ischemia, head trauma, spinal cord injury, **multiple sclerosis**, amyotrophic lateral sclerosis, Huntington's disease, Parkinson's disease, migraine, cerebral amyloid angiopathy, AIDS, age-related cognitive decline, mild cognitive impairment and prion diseases.

IT **9001-66-5**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; α-sulfonylaminohydroxamic acid inhibitors of matrix metalloproteinases for treatment of nervous system disorders, and use with other agents)

RN 9001-66-5 HCAPLUS
CN Oxidase, monoamine (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:115322 HCAPLUS
DOCUMENT NUMBER: 134:159863
TITLE: Methods of diagnosing or treating irritable bowel syndrome and other disorders caused by small intestinal bacterial overgrowth
INVENTOR(S): Lin, Henry C.; Pimental, Mark
PATENT ASSIGNEE(S): Cedars-Sinai Medical Center, USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001011077	A2	20010215	WO 2000-US22030	20000811 <--
WO 2001011077	A3	20010830		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,

CN Oxidase, monoamine (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L10 ANSWER 4 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:78560 HCAPLUS
DOCUMENT NUMBER: 134:142717
TITLE: Genotyping of the paraoxonase 1 gene for prognosing, diagnosing, and treating a disease
INVENTOR(S): Schappert, Keith
PATENT ASSIGNEE(S): Nova Molecular, Inc., Can.
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001007644	A2	20010201	WO 2000-CA830	20000719 <--
WO 2001007644	A3	20020404		
W: AU, CA, FI, JP, MX, NO, NZ, SG				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6573049	B1	20030603	US 2000-616506	20000714
EP 1208233	A2	20020529	EP 2000-945510	20000719
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				

PRIORITY APPLN. INFO.: US 1999-145602P P 19990726
WO 2000-CA830 W 20000719

AB Described herein are methods for diagnosing or treating a disease, as well as for identifying a subject for participation in a clin. trial, and identifying a subject at risk for a disease. The allele status of the PON1 gene was determined and PON1 DNA sequence polymorphisms were used to identify a subject at risk for Alzheimer's disease or non-Alzheimer's neurol. disorder.

IT **9001-66-5, Monoamine oxidase**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitor of, therapy; genotyping of paraoxonase 1 gene for prognosing and diagnosing and treating disease)

RN 9001-66-5 HCAPLUS
CN Oxidase, monoamine (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L10 ANSWER 5 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:314865 HCAPLUS
DOCUMENT NUMBER: 132:344077
TITLE: Method for determining mRNA tissue distribution using restriction endonuclease digestion and PCR amplification for database indexing and drug screening
INVENTOR(S): Hasel, Karl W.; Hilbush, Brian S.
PATENT ASSIGNEE(S): Digital Gene Technologies, Inc., USA
SOURCE: PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

ACCESSION NUMBER: 2000:260041 HCAPLUS
DOCUMENT NUMBER: 132:288782
TITLE: Methods and compositions for treating neurodegenerative diseases using an antagonist or inhibitor of p25
INVENTOR(S): Tsai, Li-Huei; Patrick, Gentry N.; Lee, Ming Sum
PATENT ASSIGNEE(S): President and Fellows of Harvard College, USA
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000021550	A2	20000420	WO 1999-US24221	19991013 <--
WO 2000021550	A3	20000727		

W: CA, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: US 1998-103975P P 19981013
US 1999-136631P P 19990527

AB The present invention relates to methods of preventing or treating neurodegenerative diseases, including Alzheimer's disease, by administering an antagonist or inhibitor of p25. In particular, the invention relates to methods of preventing or treating a neurodegenerative disease by administering a calpain antagonist or inhibitor, or a cation (e.g. Ca2+) antagonist or inhibitor, which reduces the truncation or conversion of p35 to p25. Calpeptin and ALLM, inhibitors of a calcium-activated protease (calpain), completely inhibited the conversion of p35 to p25 in calcium-treated mouse brain lysate, indicating that calpain plays an important role in the conversion process.

IT **9001-66-5, Monoamine oxidase**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; inhibition of protein p25 for treating neurodegenerative diseases)
RN 9001-66-5 HCAPLUS
CN Oxidase, monoamine (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L10 ANSWER 7 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:15421 HCAPLUS
DOCUMENT NUMBER: 132:74506
TITLE: Method for simultaneous identification of differentially expressed mRNAs and measurement of relative concentrations
PATENT ASSIGNEE(S): Scripps Research Institute, USA; Sutcliffe, J. Gregor; Erlander, Mark G.; Hasel, Karl W.
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000000646	A1	20000106	WO 1999-US14940	19990630 <--

FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000000645	A1	20000106	WO 1999-US14852	19990630 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6096503	A	20000801	US 1998-108099	19980630 <--
CA 2332339	AA	20000106	CA 1999-2332339	19990630 <--
AU 9948497	A1	20000117	AU 1999-48497	19990630 <--
EP 1092044	A1	20010418	EP 1999-932118	19990630 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002519011	T2	20020702	JP 2000-556998	19990630
US 6633818	B1	20031014	US 2000-630202	20000801
NO 2000006702	A	20010227	NO 2000-6702	20001229 <--

PRIORITY APPLN. INFO.:		
US 1998-108099	A	19980630
US 1993-152482	A3	19931112
US 1995-544577	A2	19951017
US 1998-35109	A2	19980305
US 1998-35190	A3	19980305
WO 1999-US14852	W	19990630

AB An improved method for the simultaneous sequence-specific identification of mRNAs in a mRNA population allows the visualization of nearly every mRNA expressed by a tissue as a distinct band on a gel whose intensity corresponds roughly to the concentration of the mRNA. In general, the method comprises the formation of cDNA using anchor primers to fix a 3'-endpoint, producing cloned inserts from the cDNA in a vector containing a bacteriophage-specific promoter for subsequent RNA synthesis, generating linearized fragments of the cloned inserts, preparing cRNA, transcribing cDNA from the cRNA using a set of 5'-RT primers, and performing PCR using a 3'-PCR primer whose sequence is derived from the vector and a set of 5'-PCR primers that is derived from the 5'-RT primers used for transcription of cDNA from cRNA. The method can identify changes in expression of mRNA associated with the administration of drugs or with physiol. or pathol. conditions.

IT **9001-66-5, Monoamine oxidase**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(mRNA expression pattern in response to inhibitors and stimulants of; improved method for simultaneous identification of differentially expressed mRNAs and measurement of relative concns.)

RN 9001-66-5 HCAPLUS
CN Oxidase, monoamine (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 9 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:811389 HCAPLUS
DOCUMENT NUMBER: 132:59182
TITLE: Use of BCHE genotype in the prediction of whether

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9832427	A1	19980730	WO 1998-US1556	19980127 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6309669	B1	20011030	US 1997-789734	19970127
AU 9863175	A1	19980818	AU 1998-63175	19980127 <--
PRIORITY APPLN. INFO.:			US 1997-789734 A	19970127
			US 1984-590308 B1	19840316
			US 1992-867301 A2	19920410
			US 1995-446148 A2	19950522
			US 1995-446149 B2	19950522
			US 1996-590973 B2	19960124
			WO 1998-US1556 W	19980127

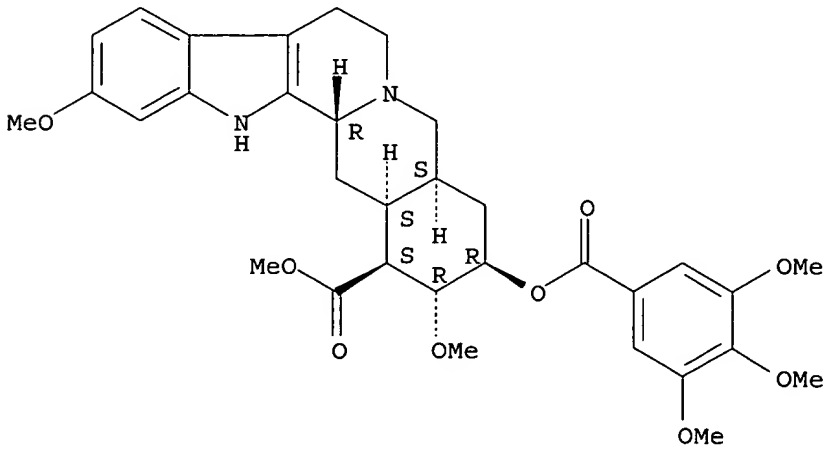
AB Novel burst-free, sustained release biocompatible and biodegradable microcapsules are disclosed which can be programmed to release their active core for variable durations ranging from 1-100 days in an aqueous physiol. environment. The microcapsules are comprised of a core of polypeptide or other biol. active agent encapsulated in a matrix of poly(lactide/glycolide) copolymer, which may contain a pharmaceutically acceptable adjuvant, as a blend of upcapped free carboxyl end group and end-capped forms ranging in ratios from 100/0 to 1/99.

IT **50-55-5, Reserpine**
RL: BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(prevention of infections with bioactive material encapsulated within biodegradable-biocompatible polymeric matrix)

RN 50-55-5 HCAPLUS

CN Yohimban-16-carboxylic acid, 11,17-dimethoxy-18-[(3,4,5-trimethoxybenzoyl)oxy]-, methyl ester, (3β,16β,17α,18.beta.,20α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
US 5668117	A	19970916	US 1993-62201	19930629	<--
CA 2166383	AA	19950112	CA 1994-2166383	19940628	<--
WO 9501096	A1	19950112	WO 1994-US7277	19940628	<--
W: AU, CA, JP					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
AU 9472144	A1	19950124	AU 1994-72144	19940628	<--
AU 692454	B2	19980611			
EP 707446	A1	19960424	EP 1994-921405	19940628	<--
R: DE, FR, GB, IT					
JP 08512055	T2	19961217	JP 1994-503597	19940628	<--
US 6746678	B1	20040608	US 2000-545870	20000406	
PRIORITY APPLN. INFO.:			US 1991-660561	B1 19910222	
			US 1993-26617	B2 19930223	
			US 1993-62201	A 19930629	
			WO 1994-US7277	W 19940628	
			US 1997-883290	B2 19970626	

OTHER SOURCE(S): MARPAT 127:288186

AB Therapeutic compns. comprising an effective amount of at least one carbonyl trapping agent alone or in combination with a therapeutically effective of a co-agent or medicament are disclosed. The compns. are used to treat a mammal suffering from a neurol. disease characterized by covalent bond crosslinking between the nerve cells, other cellular structures and their intracellular and extracellular components, with disease-induced carbonyl-containing aliphatic or aromatic hydrocarbons present in mammals.

IT **9001-66-5**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(A and B, inhibitors; carbonyl trapping agent combination with other drug for treatment of neurol. diseases and etiol. related symptomol.)

RN 9001-66-5 HCAPLUS

CN Oxidase, monoamine (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L10 ANSWER 13 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:417857 HCAPLUS

DOCUMENT NUMBER: 125:76407

TITLE: Treatment of **multiple sclerosis** (MS) and other demyelinating conditions using lofepramine in combination with L-phenylalanine, tyrosine or tryptophan and possibly a vitamin B12 compound

INVENTOR(S): Loder, Cari

PATENT ASSIGNEE(S): UK

SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9611009	A1	19960418	WO 1995-GB2361	19951005	<--
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT					
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT,					

FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9513369	A1	19950518	WO 1994-US13041	19941114	<--
W: AU, CA, FI, JP, NO, SI					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
US 5459037	A	19951017	US 1993-152482	19931112	<--
CA 2174966	AA	19950518	CA 1994-2174966	19941114	<--
AU 9510551	A1	19950529	AU 1995-10551	19941114	<--
AU 687127	B2	19980219			
EP 726946	A1	19960821	EP 1995-901229	19941114	<--
EP 726946	B1	20031001			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
JP 09509306	T2	19970922	JP 1994-514039	19941114	<--
AT 251220	E	20031015	AT 1995-901229	19941114	
FI 9602000	A	19960510	FI 1996-2000	19960510	<--
NO 9601902	A	19960712	NO 1996-1902	19960510	<--
AU 9867110	A1	19980709	AU 1998-67110	19980519	<--
AU 718304	B2	20000413			
US 6633818	B1	20031014	US 2000-630202	20000801	
US 2002127571	A1	20020912	US 2001-965561	20010925	
US 2003092006	A1	20030515	US 2001-964597	20010925	

PRIORITY APPLN. INFO.:		
US 1993-152482	A	19931112
WO 1994-US13041	W	19941114
US 1995-544577	A2	19951017
US 1998-35109	A2	19980305
US 1998-35190	A3	19980305
US 1998-108099	A1	19980630
US 1999-316349	A3	19990521

AB An improved method for the simultaneous sequence-specific identification of mRNAs in an mRNA population allows the visualization of nearly every mRNA expressed by a tissue as a distinct band on a gel whose intensity corresponds roughly to the concentration of the mRNA. In general, the method comprises the formation of cDNA using anchor primers to fix a 3'-endpoint, producing cloned inserts from the cDNA in a vector containing a bacteriophage-specific promoter for subsequent RNA synthesis, generating linearized fragments of the cloned inserts, preparing cRNA, transcribing cDNA from the cRNA using a set of primers, and performing PCR using a 3'-primer whose sequence is derived from the vector and a set of 5'-primers that is derived from the primers used for transcription of cDNA from cRNA. The method can identify changes in expression of mRNA associated with the administration of drugs or with physiol. or pathol. conditions.

IT **9001-66-5, Monoamine oxidase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors of; method for identifying changes in mRNA expression associated with administration of drugs or with physiol. or pathol. conditions)

RN 9001-66-5 HCAPLUS
CN Oxidase, monoamine (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L10 ANSWER 15 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:645253 HCAPLUS
DOCUMENT NUMBER: 123:25688
TITLE: R-enantiomer of N-propargyl-1-aminoindan, salts, compositions,and uses in treatment of nervous disorders

DOCUMENT NUMBER: 122:152
TITLE: Selective **MAO**-A and B inhibitors, radical scavengers and nitric oxide synthase inhibitors in Parkinson's disease
AUTHOR(S): Youdim, Moussa B. H.; Lavie, Lena
CORPORATE SOURCE: Dep. Pharmacol. Anatomy, Bruce Rappaport Fac. Medicine, Haifa, Israel
SOURCE: Life Sciences (**1994**), 55(25/26), 2077-82
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

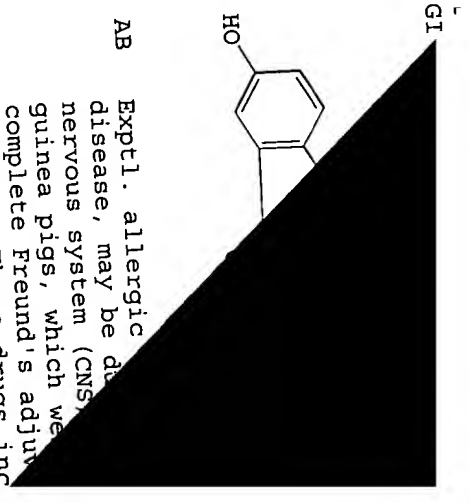
AB A review with 31 refs. In the absence of identification of either an endogenously or an exogenously derived dopaminergic neurotoxin, the most valid hypothesis currently envisaged for etiopathol. of Parkinson's disease (PD) is selective oxidative stress (OS) in substantia nigra (SN). Although OS is not proved, a significant body of evidence from studies on animal and Parkinsonian brain neurochem. supports it. This hypothesis is based on excessive formation of reactive oxygen species (O-2 and OH.) and demise of systems involved with scavenging or preventing the formation of such radicals from H2O2, generated as a consequence of dopamine oxidation (autoxidn. and deamination). Since **MAO** (**monoamine oxidase**) A and B are the major H2O2 generating enzymes in the SN, much attention has been paid to their selective inhibitors as symptomatic and neuroprotective agents in PD. Attention should also be given to radical scavengers (e.g. iron chelators, lipid peroxidative inhibitors and Vitamin E derivs.) as therapeutic neuroprotective agents in PD. This is considered valid since a significant elevation of iron is known to occur selectively in SN zone compacta and within the remaining melanized dopamine neurons of Parkinsonian brains. Although all the mechanism of iron induced oxygen free radical formation is not fully known there is no doubt that it participates with H2O2 (Fenton chemical) to generate cytotoxic hydroxyl radical (OH) and induce tissue OS and neurodegeneration in 6-hydroxydopamine model of PD. The dramatic proliferation of reactive amoeboid macrophages and microglia seen in SN of PD brains together with OS is highly compatible with an inflammatory process, similar to what has been observed in Alzheimer's disease and **multiple sclerosis** brains. This has led us to exami[illegible] produce oxygen free radicals in [illegible] latter radical has been implicate[illegible] neurons innervating the striatum [illegible] reactive macrophages NO acts as a[illegible] can synergize with dopamine oxida[illegible]

IT **9001-66-5**
RL: BSU (Biological study, unclas[illegible]
(A and B, inhibitors; selectiv[illegible]
radical scavengers and nitric [illegible]
disease)

RN 9001-66-5 HCAPLUS
CN Oxidase, monoamine (9CI) (CA INDI[illegible]

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L10 ANSWER 17 OF 19 HCAPLUS COPYRIGH[illegible]
ACCESSION NUMBER: 1984:712 HCAP[illegible]
DOCUMENT NUMBER: 100:712
TITLE: Treatment of a[illegible]
INVENTOR(S): Lieb, Julian [illegible]
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 4 pp.



AB Exptl. allergic [illegible] disease, may be d[illegible] nervous system (CNS) guinea pigs, which we[illegible] complete Freund's adju[illegible] levels. These drugs inc[illegible] [73-22-3], and carbidopa

reserpine [50-55-5] which decreases it. All immunized animals treated with saline only died, and animals treated with **reserpine** died even more quickly. A significant proportion of animals treated with the other 3 drugs, alone or in combination, survived or lived longer than controls. If a possible blockade in I transmission in EAE and **multiple sclerosis** were demonstrated, these drugs may be useful in patients with **multiple sclerosis**

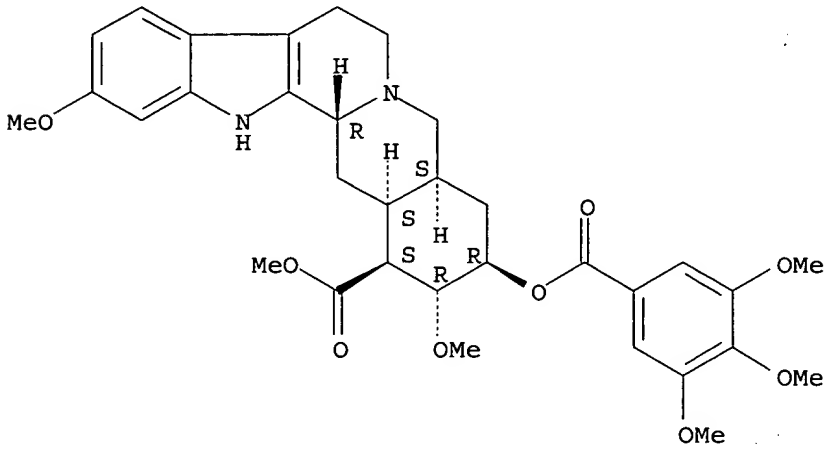
.

IT **50-55-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(serotonin of central nervous system response to, allergic encephalitis in relation to)

RN 50-55-5 HCAPLUS

CN Yohimban-16-carboxylic acid, 11,17-dimethoxy-18-[(3,4,5-trimethoxybenzoyl)oxy]-, methyl ester, (3β,16β,17α,18.beta.,20α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L10 ANSWER 19 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1965:457203 HCAPLUS
DOCUMENT NUMBER: 63:57203
ORIGINAL REFERENCE NO.: 63:10474e-g
TITLE: Histo-enzymic aspects of **multiple sclerosis**
AUTHOR(S): Giacomo, Piero De
CORPORATE SOURCE: Osp. Psichiat. Provinciale S. Maria Della Pieta, Rome
SOURCE: Lavoro Neuropsichiat. (**1964**), 35(3), 413-32
DOCUMENT TYPE: Journal
LANGUAGE: Italian

AB DPN diaphorase (I), **monoamine oxidase** (II), acid and alkaline phosphatases, nonspecific esterase, and cholinesterase were determined on cryostat sections in the study of a case of **multiple sclerosis.** Only I and to a lesser degree II showed any clear enzymic alteration in the foci. I in the affected sites showed an increase in the white substance of the activity of the "wall" of the focus with numerous astrocytic images and a decrease in the central part with the appearance of diffused granular formations, with only a slight number of glial elements visible. At certain points were observed characteristic

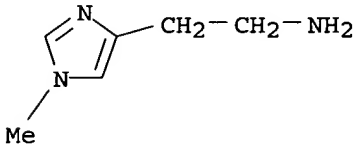
K.; Andrzejewski, W.
CORPORATE SOURCE: Institute of Biogenic Amines, Polish Academy of Sciences Lodz, Pol.
SOURCE: Journal of Physiology and Pharmacology (**2001**), 52(4, Pt. 1), 657-670
CODEN: JPHPEI; ISSN: 0867-5910
PUBLISHER: Polish Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Biochem. parameters of the histamine (HA) system were examined in both rat brain and stomach, after portocaval anastomosis (PCA). These tissues become rich in histamine after PCA. Immunocytochem. was used for brain histamine localisation. In addition to increased HA concns., **monoamine oxidase** B activity increased in both tissues. In hypothalamus HA was 15 fold; in cerebral cortex and in stomach mucosa 2.8 and 2.5 fold of the corresponding **controls**, resp. MAO B activity was increased by approx. 50% in brain and 100% in stomach. A significant, uneven increase in **tele-methylhistamine** concentration was only found in the brain. In stomach mucosa higher histidine decarboxylase activity was found. PCA and sham rats **treated** with an irreversible inhibitor of MAO B, FA-73, 0.5 mg/kg i.p., showed 24 h later greatly reduced MAO activity and doubled t-MeHA concentration in brain structures. The **treatment** had no effect on gastric mucosal t-MeHA concentration and on urinary excretion of the t-MeHA metabolite, N-tele-methylimidazoleacetic acid. The HA rise in the stomach of PCA rats is associated with proliferation of histamine producing and storing cells (ECL cells) as demonstrated by others. However, in the brain we saw no indication for increased number of relevant cells either mast cells or **neurons** and our immunocytochem. findings suggest that in PCA rat brain, histamine deposits are located exclusively in **neurons.** The data indicate that the adaptative mechanisms to excessive histamine formation are tissue specific.

IT **9001-66-5**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(B; portocaval shunt in rat results in enhanced histamine synthesis in brain and gastric mucosa resulting in higher tissue amine content)
RN 9001-66-5 HCAPLUS
CN Oxidase, monoamine (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **501-75-7**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(portocaval shunt in rat results in enhanced histamine synthesis in brain and gastric mucosa resulting in higher tissue amine content)
RN 501-75-7 HCAPLUS
CN 1H-Imidazole-4-ethanamine, 1-methyl- (9CI) (CA INDEX NAME)



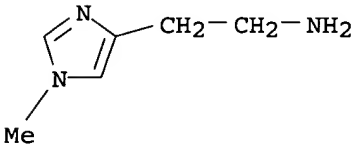
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 2 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:467468 HCAPLUS

to increase both the release and **metabolism** of **neuronal** histamine (HA). Our studies investigated the effects of several new brain-penetrating H3 antagonists on rat cerebral cortical levels of the HA metabolite **tele-methylhistamine** (t-MH). Animals were pretreated with H3 antagonists (0.3 to 30 mg/kg; 1-4 h; i.p.) in the presence or absence of the **monoamine oxidase** inhibitor pargyline to **prevent** metabolism of t-MH. Cortical t-MH levels were measured by both RIA and gas chromatog.-mass spectrometry (GC-MS). Pargyline (60 mg/kg; 1 h; i.p.) produced an .apprx.2-fold increase in t-MH levels as measured by either GC-MS or RIA. Thioperamide (± pargyline) increased t-MH levels as measured by both GC-MS and RIA. In contrast, neither 5-cyclohexyl-1-(4-imidazol-4-ylpiperidyl)pentan-1-one (GT-2016) (± pargyline), 4-(6-cyclohexylhex-cis-3-enyl)imidazole (GT-2227) (± pargyline), nor clobenpropit (minus pargyline) increased t-MH levels as measured by GC-MS. A good agreement was found between t-MH levels as determined by either RIA or GC-MS except after **treatment** with GT-2016, which increased apparent t-MH brain levels according to the former but not the latter method. Subsequent studies suggest the in vivo formation of a GT-2016 metabolite, which can cross-react in the t-MH RIA. Although all H3 receptor antagonists studied to date seem capable of enhancing brain HA release, only thioperamide presently was found to enhance cortical t-MH levels. Thus, H3 receptor antagonists may differentially affect HA release and turnover, and brain t-MH levels may not be reliable predictors of H3 agonist, partial agonist, or antagonist in vivo activity.

IT **501-75-7**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(histamine H3 receptor antagonists effect on **tele-methylhistamine** levels in cerebral cortex)

RN 501-75-7 HCAPLUS
CN 1H-Imidazole-4-ethanamine, 1-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 4 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:153068 HCAPLUS
DOCUMENT NUMBER: 128:290489
TITLE: R-(-)-α-methyl-histamine has nitric oxide-mediated vasodilator activity in the mesenteric vascular bed of the cat
AUTHOR(S): Champion, Hunter C.; Kadowitz, Philip J.
CORPORATE SOURCE: 1430 Tulane Avenue, School of Medicine, Department of Pharmacology SL83, Tulane University, New Orleans, LA, 70112, USA
SOURCE: European Journal of Pharmacology (**1998**), 343(2/3), 209-216
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

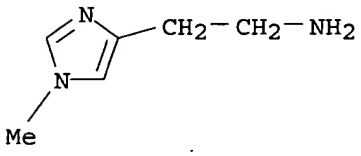
caused a reduction in arterial pressure, which was antagonized by famotidine, no pressor response being unmasked. Dimaprit (0.1-30 μmol/kg i.v.) did not modify heart rate but caused a modest bradycardia at 100 μmol/kg i.v. Amthamine (1-100 μmol/kg i.v.) induced a dose-dependent tachycardia, which was only partially (approx. 20%) reduced by famotidine and was totally blocked by propranolol (0.3 mg/kg i.v.). This effect was significantly reduced in rats pretreated with **reserpine** or 6-hydroxydopamine and was further reduced by cocaine, thus suggesting a tyramine-like action of amthamine. In conclusion, these data demonstrate that the **H2** receptor **agonist** amthamine can also interact with the adrenergic system when used at doses higher than those necessary to activate **H2** receptors. Whereas the increase in blood pressure induced by amthamine seems to be mainly mediated by a direct activation of postjunctional α2 adrenoceptors, the increase in heart rate is predominantly due to **neuronal** release of catecholamines. These effects should be considered when using amthamine in cardiovascular or other studies when high doses are employed.

L26 ANSWER 6 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:118482 HCAPLUS
DOCUMENT NUMBER: 124:250525
TITLE: Effects of the histamine H3 agonist (R)-α-methylhistamine and the antagonist thioperamide in vitro on **monoamine oxidase** activity in the rat brain
AUTHOR(S): Sakurai, E.; Sakurai, E.; Maeyama, K.; Watanabe, T.; Jossan, S.S.; Oreland, L.
CORPORATE SOURCE: Department of Pharmaceutics I, Tohoku College of Pharmacy, Sendai, Japan
SOURCE: Methods and Findings in Experimental and Clinical Pharmacology (**1995**), 17(Suppl. C), 46-50
CODEN: MFEPDX; ISSN: 0379-0355
PUBLISHER: Prous
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of an H3 agonist, (R)-α-methylhistamine (α-MeHA), and an H3 antagonist, thioperamide, on **monoamine oxidase** (MAO) activity in rat hypothalamus were studied in vitro. Thioperamide was more potent in inhibiting MAO-B than MAO-A activity; MAO-B activity in rat hypothalamic homogenates was competitively inhibited by thioperamide with a Ki value of 175 μM. From this in vitro experiment, the conversion of N-**telemethylhistamine** to N-tele-methylimidazoleacetic acid may be inhibited by thioperamide, suggesting that thioperamide may affect the regulation of histamine **metabolism** within histaminergic **neurons.** In contrast with the results obtained with thioperamide, α-MeHA inhibited MAO-A more potently than MAO-B activity; the Ki values for MAO-A and -B of hypothalamic homogenates were estimated to be 1.1 and 3.3 mM, resp. The weak inhibitory effect of α-MeHA for MAO-B does not seem to be a major cause of changes in N-**tele-methylhistamine** concns.
IT **501-75-7 9001-66-5, Monoamine oxidase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(effects of the histamine H3 agonist (R)-α-methylhistamine and the antagonist thioperamide in vitro on **monoamine oxidase** activity in the rat brain)
RN 501-75-7 HCAPLUS
CN 1H-Imidazole-4-ethanamine, 1-methyl- (9CI) (CA INDEX NAME)

distribution of MAO-B in human brain by autoradiog. use of 11C-L-deprenyl was high in the caudate nucleus, putamen, thalamus, and substantia nigra. The half-life for the turnover rate of MAO-B in pig brain by positron emission tomog. using 11C-L-deprenyl was calculated to be 6.5 days. The relation between serotonin and dopamine uptake rates, monoamine concns. and MAO activities was estimated in various regions of rat brain. Of main interest is the finding that MAO activities in general (conventional method) were pos. correlated to serotonin uptake rates and to intra-5-HT-synaptosomal MAO, but not to dopamine uptake rates or intra-DA-synaptosomal MAO activities. An inhibition of MAO-B of more than 40% was required to reduce the MPTP toxicity and it was completely **prevented** at about 60% MAO inhibition. Moreover, although MPTP toxicity in relation to age, dopamine uptake and MAO activity was investigated in two rodent species, MAO-B activity was not the rate-limiting step for MPTP **neurotoxicity.** Histamine H3-ligands inhibited the conversion of N-**tele-methylhistamine** to N-tele-methylimidazoleacetic acid by MAO-B in the rat brain. The oxidation of racemic chlorpheniramine was catalyzed by mitochondrial MAO of rat brain. Moreover, there was a stereoselective difference in oxidative deamination of chlorpheniramine by MAO-A and -B.

IT **9001-66-5, Monoamine oxidase**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(B, amine metabolism by and specificity of **monoamine oxidase** of mitochondria of brain of human and laboratory animals)
RN 9001-66-5 HCAPLUS
CN Oxidase, monoamine (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **501-75-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(N-telemethylimidazoleacetic acid formation from methylhistamine by brain **monoamine oxidase** inhibition by histaminergic H3 ligands)
RN 501-75-7 HCAPLUS
CN 1H-Imidazole-4-ethanamine, 1-methyl- (9CI) (CA INDEX NAME)

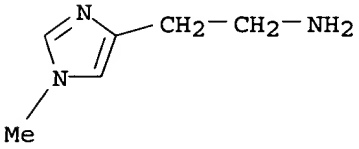


L26 ANSWER 9 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:157791 HCAPLUS
DOCUMENT NUMBER: 120:157791
TITLE: Identification of unusual polyamines by the combined use of high-performance liquid chromatography and polyamine-metabolizing enzymes
AUTHOR(S): Matsuzaki, Shigeru; Hamana, Koei; Okada, Masato; Isobe, Kimiyasu
CORPORATE SOURCE: Sch. Med., Dokkyo Univ., Mibu, 321-02, Japan
SOURCE: Dokkyo Journal of Medical Sciences (**1992**), 19(2), 117-24
CODEN: DJMSDB; ISSN: 0385-5023

acid (HVA) were more than doubled. The net increase in t-MeHA concentration in response to pargyline (80 mg/kg i.p.) was almost the same for PCA and sham-operated rats. This implies that the great enhancement of the histamine level in this area might be a consequence of the persistent stimulation of its synthesis and the unchanged activity of histaminergic **neurons.** In the rest of the brain, the steady-state level of t-MeHA was higher after PCA (3.8-fold), as were the levels of 5-HIAA and HVA. Surprisingly, t-MeHA remained unchanged after **monoamine oxidase** blockade. Of the pargyline-induced alterations in the concns. of indoles and catechols, the most pronounced were those in the 5-HT level; 5-HT was elevated >2-fold in hypothalamus and >12-fold in the rest of the brain, with a concomitant 80% decrease in 5-HIAA. The dopamine and, to a much smaller extent, noradrenaline levels were also increased, and the levels of HVA and 3,4-dihydroxyphenylacetic acid fell below the detection limit. Apparently, at least 2 different mechanisms operate in the brains of PCA rats to counteract the excessive synthesis of **neuromediators**, e.g., increased deposition and increased metabolism

IT **9001-66-5**, MAO
RL: BIOL (Biological study)
(B, inhibition of, methylhistamine in brain and hypothalamus response to, portocaval shunting effect on, amine **neurotransmitters** in relation to)
RN 9001-66-5 HCAPLUS
CN Oxidase, monoamine (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **501-75-7**, N-**tele-Methylhistamine**
RL: BIOL (Biological study)
(in brain and hypothalamus, portocaval shunting and MAO B inhibition effect on)
RN 501-75-7 HCAPLUS
CN 1H-Imidazole-4-ethanamine, 1-methyl- (9CI) (CA INDEX NAME)



L26 ANSWER 11 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:70063 HCAPLUS
DOCUMENT NUMBER: 120:70063
TITLE: Histamine inhibits spontaneous activity of the uterus of the progesterone-**treated** rat
AUTHOR(S): Rubio, E.; Estan, L.; Morales-Olivas, F. J.; Martinez-Mir, M. I.
CORPORATE SOURCE: Fac. Med. Odontol., Univ. Valencia, Valenica, 46010, Spain
SOURCE: Journal of Autonomic Pharmacology (**1993**), 13(6), 395-402
CODEN: JAPHDU; ISSN: 0144-1795
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of i.v. administered histamine, and its analogs, 4-methylhistamine and 2-pyridylethylamine, on the spontaneous activity of the progesterone-**treated** rat uterus were examined in vivo. The inhibitory effect of adrenaline was also studied. These **agonists**

deferentia preloaded with [3H]noradrenaline was investigated. The overflow evoked by the various **agonists** was unaffected by the presence of such receptor **agonists** as propranolol, phentolamine, cimetidine, or scopolamine. On the other hand, the overflow evoked by all **agonists** except dimaprit was inhibited by mepyramine and by 2 well-known **neuronal** uptake inhibitors, cocaine and desipramine. The inhibition by mepyramine has been attributed to its effect on the **neuronal** uptake process. Metabolic profile studies showed that 3,4-dihydroxyphenylglycol (DOPEG) was the major constituent in the evoked overflow caused by histamine, 2-methylhistamine, 4-methylhistamine, and dimaprit and that the overflow evoked by 2-pyridylethylamine and 2-thiazolylethylamine consisted predominantly of unchanged noradrenaline. Based on these findings, it is concluded that all of the **agonists** tested evoke noradrenaline release intraneuronally by entering the adrenergic **nerve** terminals. While dimaprit might enter by passively diffusing into the adrenergic **nerves**, other **agonists** seem to use the **neuronal** uptake process. However, there are qual. and quant. differences in the metabolic profile of the overflow evoked by various **agonists.** These differences could arise from their addnl. properties, such as their effect on the **neuronal** uptake process and (or) their ability to act as a substrate for **neuronal monoamine oxidase.**

L26 ANSWER 14 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:199557 HCAPLUS
DOCUMENT NUMBER: 114:199557
TITLE: Effect of **reserpine** on histamine metabolism in the mouse brain
AUTHOR(S): Muroi, Nobuyuki; Oishi, Ryozo; Saeki, Kiyomi
CORPORATE SOURCE: Med. Sch., Okayama Univ., Okayama, 700, Japan
SOURCE: Journal of Pharmacology and Experimental Therapeutics (**1991**), 256(3), 967-72
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English

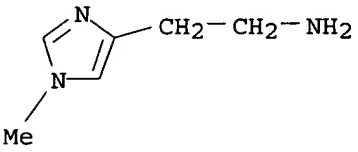
AB The effect of **reserpine** on brain histamine (HA) metabolism was examined in mice. The level of **tele-methylhistamine**, a major metabolite of HA, was decreased dose-dependently by **reserpine** (1-5 mg/kg s.c.), whereas the HA level was unaffected. This effect was observed in all brain regions examined The accumulation of **tele-methylhistamine** induced by pargyline (65 mg/kg i.p.), an inhibitor of **monoamine oxidase**, was inhibited to 19% of the **control** value 24 h after the **treatment** with **reserpine** (5 mg/kg s.c.). The HA decrease induced by (S)-α-fluoromethylhistidine (50 mg/kg i.p.), a specific inhibitor of histidine decarboxylase, was not affected by pretreatment with **reserpine** (5 mg/kg s.c.) 1 or 24 h before. The HA increase induced by metoprine (10 mg/kg i.p.), an inhibitor of histamine N-methyltransferase, or by L-histidine (0.5-1.5 g/kg i.p.) was inhibited markedly by **reserpine.** This effect was more marked when **reserpine** was administered 1 h than 24 h before. The L-histidine-induced increase in HA levels was enhanced markedly by the simultaneous administration of metoprine in the **control** mice but not in the mice **treated** with **reserpine** 1 h before L-histidine injection. There may be both **reserpine**-resistant and **reserpine**-sensitive HA pools in histaminergic **nerve** endings and most of the **neuronal** HA in the brain may be located in the former pool. The capacity of the former pool may be limited and thus most of the increased HA by L-histidine and metoprine may be transferred into the latter pool. The **reserpine**-sensitive pool

SOURCE: Brain Research (**1990**), 521(1-2), 125-30
CODEN: BRREAP; ISSN: 0006-8993
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of morphine on the levels of histamine (HA), its metabolite **tele-methylhistamine** (t-MH) and on t-MH synthesis rates (thought to be indicative of **neuronal** HA release) were investigated in brain regions and spinal cords of DBA/2J (DBA) and C57/BL6 (C57) mice, two strains known to differ in their sensitivity to morphine. In DBA (a strain highly sensitive to morphine antinociception), morphine (10 mg/kg, s.c.) had no effect on brain regional t-MH or HA levels, but produced a generalized inhibition of regional t-MH synthesis rates ranging from 11 to 53%. The **monoamine oxidase** (MAO) inhibitor pargyline (used to estimate t-MH synthesis rates) had no effect on HA or t-MH levels in the DBA or C57 spinal cord, indicating the absence of detectable spinal HA turnover. Morphine (10 mg/kg) had no effect on DBA or C57 spinal cord HA or t-MH levels, but significantly increased t-MH synthesis in the DBA but not in the C57 spinal cord. These results suggest that in DBA mice, antinociceptive doses of morphine inhibit HA release in brain, and promote the release of HA from spinal cord. Neither effect was found in C57 mice, which are resistant to morphine antinociception. The relevance of these actions to previous studies showing the blockade of opiate antinociception by H2 antagonists remains to be established.

IT **501-75-7, tele-Methylhistamine**
RL: BIOL (Biological study)
(as histamine metabolite, in brain vs. spinal cord, morphine effect on)

RN 501-75-7 HCAPLUS
CN 1H-Imidazole-4-ethanamine, 1-methyl- (9CI) (CA INDEX NAME)



L26 ANSWER 16 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1990:787 HCAPLUS
DOCUMENT NUMBER: 112:787
TITLE: Sensitive radioimmunoassays for histamine and **tele-methylhistamine** in the brain
AUTHOR(S): Garbarg, M.; Pollard, H.; Trung Tuong, My Dam; Schwartz, J. C.; Gros, C.
CORPORATE SOURCE: Unite Neurobiol. Pharmacol., Cent. Paul Broca, Paris, 75014, Fr.
SOURCE: Journal of Neurochemistry (**1989**), 53(6), 1724-30
CODEN: JONRA9; ISSN: 0022-3042
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Serum albumin conjugates of histamine or **tele-methylhistamine**, a major catabolite, were prepared using 1,4-benzoquinone as the coupling agent and were used to raise polyclonal antibodies in rabbits. The same reagent was used to prepare the [125I]iodinated tracer and **treat** tissue exts. submitted to the RIAs. The IC50 values of prederivatized histamine and **tele-methylhistamine** in the RIAs were 0.3 nM and 0.5 nM, resp., whereas nonderivatized histamine or **tele-methylhistamine**,

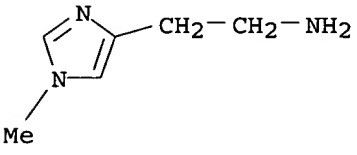
kappa-selective opioid **agonist** U-50,488H produced a dose-dependent increase in gastric acid secretion after i.v. but not i.c.v. administration. Other kappa-selective **agonists** tested did not produce a significant increase in gastric acid secretion after i.c.v. or i.v. administration. The increase in gastric acid secretion produced by U-50,488H was blocked by **treatment** with the opioid receptor antagonist naloxone, the nonselective muscarinic receptor antagonist atropine, and the M1 selective muscarinic receptor antagonist pirenzepine. The secretory effects of U-50,488H were not blocked by pretreatment with the ganglionic blocker hexamethonium, the **H2** receptor antagonist metiamide, **reserpine**, or the sep. or combined action of the alpha and beta adrenergic receptor antagonists phentolamine and propranolol, resp. Thus, stimulation of central and possibly peripheral mu opioid receptors in rats apparently decreases gastric acid secretion, whereas delta opioid receptors are not involved in the mediation of gastric acid secretion. U-50,488H, a kappa-selective opioid **agonist**, may increase gastric acid secretion by a mechanism which involves the local release of acetylcholine acting on M1 receptors on the parietal cell to secrete acid.

L26 ANSWER 18 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1986:530279 HCAPLUS
DOCUMENT NUMBER: 105:130279
TITLE: Electrostatic potential comparison and molecular metric spaces
AUTHOR(S): Carbot, Ramon; Sune, Eduard; Lapena, Felix; Perez, Jose
CORPORATE SOURCE: Dep. Quimiometria, Inst. Quim. Sarria, Barcelona, 08017, Spain
SOURCE: Journal of Biological Physics (**1986**), 14(1), 21-8
CODEN: JBPHBZ; ISSN: 0092-0606
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A possible definition of a metric associated with a set of electrostatic mol. potentials was analyzed in relation to **pharmacol.** or biol. activities of substances and methods of studying those properties. Examples of its application to HCHO and analogous structures and to **monoamine oxidase** substrates are presented.

IT **501-75-7**
RL: PRP (Properties)
(electrostatic potential and mol. metric space of, **monoamine oxidase** in relation to)

RN 501-75-7 HCAPLUS
CN 1H-Imidazole-4-ethanamine, 1-methyl- (9CI) (CA INDEX NAME)



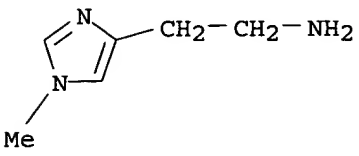
IT **9001-66-5**
RL: ANST (Analytical study)
(substrates of, electrostatic potential and mol. metric space of)

RN 9001-66-5 HCAPLUS
CN Oxidase, monoamine (9CI) (CA INDEX NAME)

ones. The inhibitors could potentiate food poisoning caused by histamine by inhibiting its metabolism

IT **501-75-7**
RL: BIOL (Biological study)
(histamine metabolite, formation of, **pharmacol.** and food borne inhibitors effect on)

RN 501-75-7 HCAPLUS
CN 1H-Imidazole-4-ethanamine, 1-methyl- (9CI) (CA INDEX NAME)



L26 ANSWER 21 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1984:97268 HCAPLUS
DOCUMENT NUMBER: 100:97268
TITLE: Histamine turnover in regions of rat brain
AUTHOR(S): Hough, Lindsay B.; Khandelwal, J. K.; Green, Jack Peter
CORPORATE SOURCE: Mt. Sinai Sch. Med., City Univ. New York, New York, NY, 10029, USA
SOURCE: Brain Research (**1984**), 291(1), 103-9
CODEN: BRREAP; ISSN: 0006-8993
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Rapid and complete inhibition of **monoamine oxidase** by pargyline produced linear increases in the content of the histamine [51-45-6] metabolite **tele-methylhistamine** (t-MH) [**501-75-7**] in 9 regions of rat brain 2 and 4 h after **drug** administration. The **treatment** had little or no effect on the histamine content of these regions. As histamine methylation is the major metabolic pathway of histamine in the brain, the rate of increase in brain t-MH content after complete inhibition of its metabolism provides an estimate of histamine turnover. Histamine turnover rates varied >46-fold among regions, from cerebellum (0.029 nmol/g/h) to hypothalamus (1.33 nmol/g/h), similar to reports for norepinephrine and serotonin. Turnover rates were highly correlated with **control** t-MH levels and **control** histamine levels. Rate consts. were highest in the caudate nucleus and frontal cortex, equivalent to a half-life of .apprx.11 min in these regions. Although hypothalamic histamine had the highest turnover rate, the rate constant for histamine in this region was among the lowest in the brain, perhaps consistent with the presence of histaminergic cell bodies. Histamine turnover rates may be indicative of the activity of histamine-synthesizing **neurons**, and its determination will facilitate understanding of histamine in the brain.

IT **501-75-7**
RL: BIOL (Biological study)
(of brain regions, histamine metabolism in relation to)

RN 501-75-7 HCAPLUS
CN 1H-Imidazole-4-ethanamine, 1-methyl- (9CI) (CA INDEX NAME)

DOCUMENT NUMBER: 98:84038
TITLE: Effect of yohimbine on rat prolactin secretion
AUTHOR(S): Meltzer, Herbert Y.; Simonovic, Miljana; Gudelsky, Gary A.
CORPORATE SOURCE: Pritzker Sch. Med., Univ. Chicago, Chicago, IL, 60637, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (**1983**), 224(1), 21-7
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English

AB yohimbine (YOH) [146-48-5] produced marked, dose-dependent, and sustained increases in plasma prolactin (PRL) [9002-62-4] levels in male rats. However, YOH did not block the inhibitory effect of dopamine (DA) [51-61-6] on PRL release from rat pituitary glands in vitro, did not displace 3H-labeled spiperone [749-02-0] from bovine pituitary membranes, and had no effect on the concentration of DA in pituitary stalk plasma of anesthetized rats, suggesting that the stimulation of PRL release by YOH is not due to its antidopaminergic effects. Clonidine, an α-adrenergic **agonist**, produced a partial, non-dose-dependent inhibition of the YOH-induced rise in serum PRL levels. Two antagonists of the H1 histamine [51-45-6] receptor, diphenhydramine and promethazine, markedly antagonized the PRL-releasing effect of YOH, but another H1 blocker, chlorpheniramine, and an **H2** antagonist, metiamide, had no effect. serotonin [50-67-9] Receptor blockers, cyproheptadine, mianserin, and pizotifen, and the opiate antagonist, naloxone, also had no effect on the PRL response to YOH. Nevertheless, the PRL-releasing effect of YOH was potentiated 24 h after the administration of **reserpine** or p-chlorophenylalanine, an inhibitor of serotonin synthesis. Thus, the mechanisms by which YOH stimulates rat PRL secretion have not been fully elucidated. It is possible that YOH may stimulate PRL secretion by a novel mechanism, possibly through the intervention of a PRL-releasing factor.

L26 ANSWER 24 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1983:46883 HCAPLUS
DOCUMENT NUMBER: 98:46883
TITLE: Effects of pargyline on **tele-methylhistamine** and histamine in rat brain
AUTHOR(S): Hough, Lindsay B.; Khandelwal, Jai K.; Green, Jack Peter
CORPORATE SOURCE: Mt. Sinai Sch. Med., City Univ. New York, New York, NY, 10029, USA
SOURCE: Biochemical Pharmacology (**1982**), 31(24), 4074-6
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In rats rapid and complete inhibition of brain **monoamine oxidase** (MAO) [**9001-66-5**] by pargyline [555-57-7] produced linear increases in brain **tele-methylhistamine** (t-MH) [**501-75-7**] levels from 30 min to 4 h after **drug treatment** at 0.26 nmole/g/h resulting in a 3-fold increase which persisted for at least 12 h. histamine (HA) [51-45-6] levels were slightly elevated 1 and 2 h after **drug** administration but quickly returned to **control** levels, suggestive of sensitive regulatory mechanisms in brain. Although the slight change in HA levels precludes steady-state assumptions, the rate of increase in brain t-MH levels after MAO inhibition provides a novel estimate of the half-life of endogenous brain HA (50 min). Despite the transient effect of pargyline

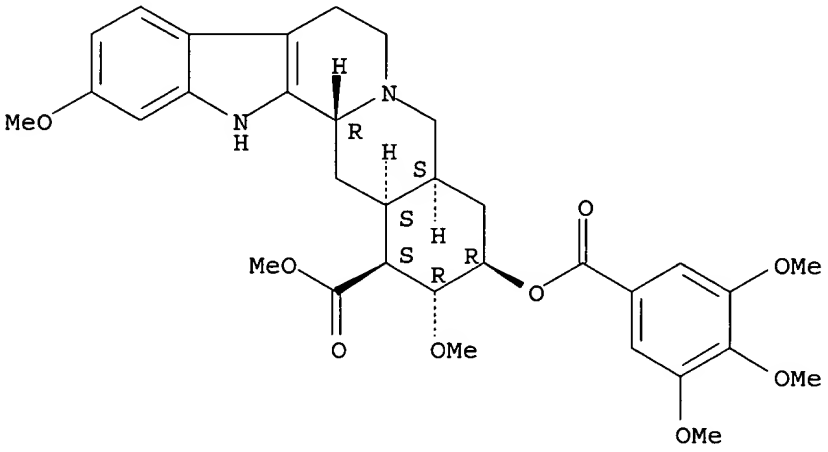
β-blocking agents metoprolol [37350-58-6] (cardioselective) or Th 326 [83764-80-1] (non-cardioselective) during the whole postinfarction period. A reduction of infarct size could be established for metoprolol (-33%), for **reserpine** (-27%), and for Th 326 (-14%). Apparently, the abnormalities observed in the non-ischemic surviving myocardium are the result of a specific damage of sarcolemmal β-receptors due to post-MI excessive levels of circulating catecholamines. This impairment can be effectively **prevented** by **treatment** with β-blocking agents. Furthermore, the possible risk of β-blocker-induced heart failure can be avoided if cardiac contractility is stimulated via the **H2**-receptor-adenylate cyclase system which was found to exist in the human myocardium as well with very similar receptor kinetics and properties.

IT **50-55-5**
RL: BIOL (Biological study)
(heart infarct size minimization by, catecholamine-induced β-adrenergic receptor damage in relation to)

RN 50-55-5 HCAPLUS

CN Yohimban-16-carboxylic acid, 11,17-dimethoxy-18-[(3,4,5-trimethoxybenzoyl)oxy]-, methyl ester, (3β,16β,17α,18.beta.,20α)- (9CI) (CA INDEX NAME)

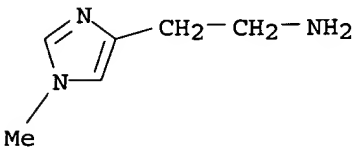
Absolute stereochemistry. Rotation (-).



L26 ANSWER 26 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1981:455218 HCAPLUS
DOCUMENT NUMBER: 95:55218
TITLE: **Pharmacological** investigations into the effects of histamine and histamine analogs on guinea pig and rat uterus
AUTHOR(S): Goyal, Ramesh K.; Verma, Subhash C.
CORPORATE SOURCE: Dep. Pharmacol., I. M. Coll. Pharm., Ahmedabad, 380009, India
SOURCE: Agents and Actions (**1981**), 11(4), 312-17
CODEN: AGACBH; ISSN: 0065-4299
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

elevated levels of SAM.
IT **9001-66-5**
RL: BIOL (Biological study)
(B, of brain in histamine catabolism, adenosylmethionine effect on)
RN 9001-66-5 HCAPLUS
CN Oxidase, monoamine (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **501-75-7**
RL: FORM (Formation, nonpreparative)
(formation of, from histamine by brain, adenosylmethionine effect on)
RN 501-75-7 HCAPLUS
CN 1H-Imidazole-4-ethanamine, 1-methyl- (9CI) (CA INDEX NAME)



L26 ANSWER 28 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1980:465027 HCAPLUS
DOCUMENT NUMBER: 93:65027
TITLE: Determination of urinary methylhistamine excretion in male and female rats by gas chromatography with electron-capture detection
AUTHOR(S): Doshi, Pravin S.; Edwards, David J.
CORPORATE SOURCE: Sch. Dent. Med., Univ. Pittsburgh, Pittsburgh, PA, 15261, USA
SOURCE: Life Sciences (**1980**), 26(23), 1947-53
CODEN: LIFSAK; ISSN: 0024-3205
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A gas-liquid chromatog. method for the determination of methylhistamine in urine is described. Methylhistamine is reacted with 2,6-dinitro-4-trifluoromethylbenzenesulfonic acid and the derivative thus formed is quantitated with electron-capture detection. The 24-h urinary excretion of methylhistamine in the male rat is .apprx.5-fold greater than that in the female rat. Aminoguanidine, a diamine oxidase inhibitor, causes a 4-5-fold increase in methylhistamine excretion in both male and female rats. **Treatment** with pargyline, a **monoamine oxidase** inhibitor, causes only a small increase in methylhistamine excretion in male and female rats, thereby suggesting that oxidative deamination of methylhistamine is a relatively minor pathway.
IT **501-75-7**
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in urine anal. by gas chromatog. with electron-capture detection)
RN 501-75-7 HCAPLUS
CN 1H-Imidazole-4-ethanamine, 1-methyl- (9CI) (CA INDEX NAME)

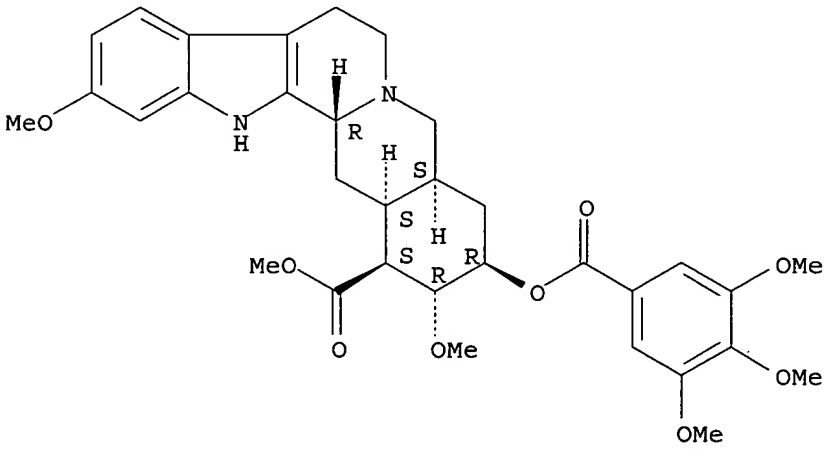
AB The ulcerogenic and secretogenic properties of betazole-HCl (I) [138-92-1] (a histaminic **H2 agonist**) and **reserpine** [**50-55-5**] on pig stomachs were studied. I (50 mg/body) and **reserpine** (0.02 mg/kg) were successively injected (i.m.) daily for 5-10 days into starved animals. Gastroesophageal ulcers, pathol. similar to naturally occurring ulcers, were observed in all pigs whether a nutrient solution (5% glucose, 1L/day) was supplied or not. In starved pigs given either I or **reserpine**, only a small ulcer or erosion was observed In 4 pigs given com. mash at a rate of 3% of body weight/day and killed on the 6th or 10th day of successive injections of both **drugs**, the incidence of ulcers was 2/4. The gastric secretogenc effect of I and/or **reserpine** was confirmed in pigs with Heidenhain gastric pouches. From these data, a new method for the exptl. induction of pig gastroesophageal ulcers by simultaneous injections of I and **reserpine** for 5 days under the nutrient (glucose solution) drinking condition, is proposed. This method may be superior to the repository histamine method, with respect to the absence of adverse effects, practical convenience, and pathol. and etiol. similarities with naturally occurring ulcers.

IT **50-55-5**
RL: BIOL (Biological study)
(esophagogastric ulcer from betazole and)

RN 50-55-5 HCAPLUS

CN Yohimban-16-carboxylic acid, 11,17-dimethoxy-18-[(3,4,5-trimethoxybenzoyl)oxy]-, methyl ester, (3β,16β,17α,18.beta.,20α)- (9CI) (CA INDEX NAME)

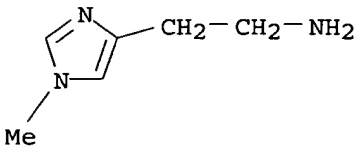
Absolute stereochemistry. Rotation (-).



L26 ANSWER 31 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1979:201109 HCAPLUS
DOCUMENT NUMBER: 90:201109
TITLE: **Tele-Methylhistamine** oxidation by type B **monoamine oxidase**
AUTHOR(S): Hough, Lindsay B.; Domino, Edward F.
CORPORATE SOURCE: Dep. Pharmacol., Univ. Michigan, Ann Arbor, MI, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (**1979**), 208(3), 422-8
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal

decarboxylase [9024-61-7] inhibitors. Urinary methylhistamine [**501-75-7**] excretion was increased .apprx.3-fold in rats **treated** simultaneously with the histaminase inhibitor aminoguanidine [79-17-4] and the **monoamine oxidase** inhibitor pargyline [555-57-7], thus providing a high base-line against which inhibition of methylhistamine formation, and hence of histamine [51-45-6] formation, could be measured. Variations in the recovery of methylhistamine were compensated for by addition of a standard amount of radioactive methylhistamine to each urine sample. The method has the advantage over previously described methods of requiring less radioactive material and fewer animals which, moreover, do not have to be killed and so can be re-used. In addition, the time course of inhibition can be assessed.

IT **501-75-7**
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in urine, histidine decarboxylase inhibitors in relation to)
RN 501-75-7 HCAPLUS
CN 1H-Imidazole-4-ethanamine, 1-methyl- (9CI) (CA INDEX NAME)



L26 ANSWER 33 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1978:186766 HCAPLUS
DOCUMENT NUMBER: 88:186766
TITLE: Methylhistamine. Evidence for selective deamination by MAO B in the rat brain in vivo
AUTHOR(S): Waldmeier, P. C.; Feldtrauer, J. J.; Maitre, L.
CORPORATE SOURCE: Res. Dep., Ciba-Geigy Ltd., Basel, Switz.
SOURCE: Journal of Neurochemistry (**1977**), 29(5), 785-90
CODEN: JONRA9; ISSN: 0022-3042
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Solvent extraction and subsequent thin-layer chromatog. showed that after intracisternal injection of labeled histamine into rat brain 40-3% of the label was detected as methylhistamine (I) and 28-30% was methylimidazoleacetic acid (II). Deprenil and pargyline (50 mg/kg, s.c.) increased I levels ≤150% and decreased II levels to 10% of **controls**; clorgyline (≤10 mg/kg, s.c.) had no effect on I and II levels. Recovery from pargyline occurred within 21 days and the half-lives observed with I and II were 5.3 and 5.6 days resp. I is metabolized selectively by **monoamine oxidase** B and may be a more selective substrate than phenylethylamine.

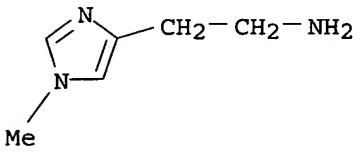
IT **9001-66-5**
RL: BIOL (Biological study)
(B, of brain, methylhistamine deamination by)
RN 9001-66-5 HCAPLUS
CN Oxidase, monoamine (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **501-75-7**
RL: RCT (Reactant); RACT (Reactant or reagent)

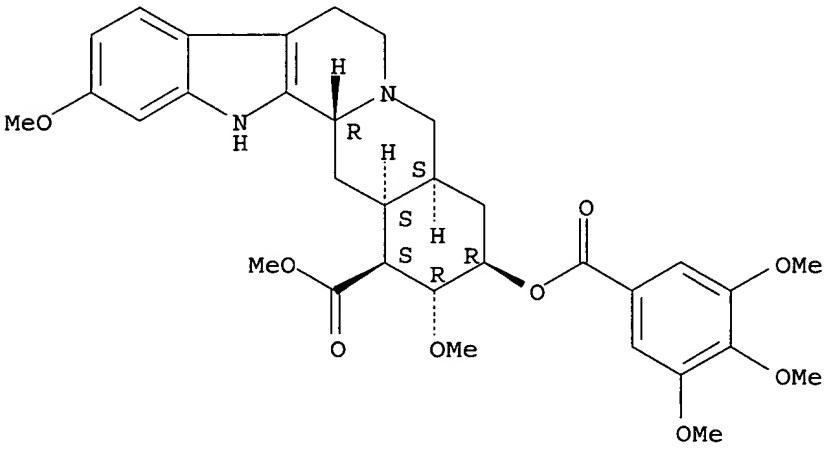
increased the concns. of 14C-labeled histamine and methylhistamine [**501-75-7**] 2 hr after intracerebral injection of histamine-14C. Imipramine [50-49-7], reduced the levels of labeled histamine. None of the **drugs** tested, however, increased the levels of labeled histamine 30 min after intracerebral injection of L-histidine [71-00-1].

IT **501-75-7**
RL: FORM (Formation, nonpreparative)
(formation of, from histamine, by brain, psychoactive **drugs** effect on)
RN 501-75-7 HCAPLUS
CN 1H-Imidazole-4-ethanamine, 1-methyl- (9CI) (CA INDEX NAME)



IT **50-55-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(histamine metabolism by brain response to)
RN 50-55-5 HCAPLUS
CN Yohimban-16-carboxylic acid, 11,17-dimethoxy-18-[(3,4,5-trimethoxybenzoyl)oxy]-, methyl ester, (3β,16β,17α,18.beta.,20α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

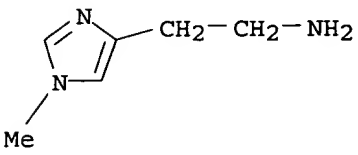


L26 ANSWER 36 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1972:121760 HCAPLUS
DOCUMENT NUMBER: 76:121760
TITLE: Catabolism of [3H]-histamine in the rat brain after intracisternal administration
AUTHOR(S): Schwartz, Jean Charles; Pollard, Helene; Bischoff, Serge; Rehault, Marie C.; Verdiere-Sahuque, Martine
CORPORATE SOURCE: Lab. Biochim., Hop. Broca, Paris, Fr.
SOURCE: European Journal of Pharmacology (**1971**), 16(3), 326-35

of histidine decarboxylase, failed to affect histamine catabolism. There was no evidence of parallelism between the histamine-destroying enzymes and the histamine-forming enzyme, histidine decarboxylase, either in distribution or ability to undergo changes in activity. No support was obtained for the view that histamine-catabolizing enzymes play a role in the local **control** of responses to newly formed histamine.

IT **501-75-7**
RL: BIOL (Biological study)
(histamine metabolism inhibition by)

RN 501-75-7 HCAPLUS
CN 1H-Imidazole-4-ethanamine, 1-methyl- (9CI) (CA INDEX NAME)



L26 ANSWER 38 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1970:484266 HCAPLUS
DOCUMENT NUMBER: 73:84266
TITLE: Potentiation of responses to histamine in aortic strips by steroids
AUTHOR(S): Kalsner, Stanley
CORPORATE SOURCE: Dep. Pharmacol., Univ. Ottawa, Ottawa, Can.
SOURCE: Canadian Journal of Physiology and Pharmacology (**1970**), 48(7), 443-9
CODEN: CJPPA3; ISSN: 0008-4212
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Responses to histamine were potentiated by 17β-estradiol in untreated and **reserpine-treated** aortic strips. 17β-Estradiol produced significantly greater potentiation after inhibition of diamine oxidase with iproniazid. Amodiaquine and quinidine, 2 known inhibitors of imidazole N-methyltransferase, enhanced responses to histamine and abolished the potentiating effect of 17β-estradiol. Also, contractions produced by histamine were not increased by amodiaquine or quinidine in the presence of 17β-estradiol. Responses to histamine were increased only slightly by testosterone and hydrocortisone, and these effects were also blocked by known inhibitors of N-methylation. Responses to 1,4-methylhistamine, the N-methylated metabolite of histamine, were not enhanced by 17β-estradiol or amodiaquine, and in only 1 of 6 strips by quinidine. Studies with the oil immersion technique indicated that imidazole N-methyltransferase is a major mechanism terminating the action of histamine in aortic strips. The rate of N-methylation was significantly decreased by amodiaquine, quinidine, and 17β-estradiol. It is concluded that the steroid hormones enhance responses of vascular tissue to histamine by inhibiting N-methylation. Contractions of rabbit ileum by histamine were not increased by 17β-estradiol, perhaps owing to a dominant depressant effect of the steroid on the amplitude of spontaneous contractions.

IT **501-75-7**
RL: BIOL (Biological study)
(arteries response to, steroid potentiation of histamine action in relation to)

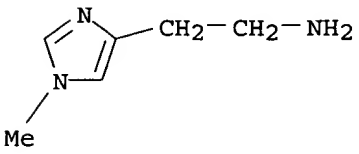
RN 501-75-7 HCAPLUS
CN 1H-Imidazole-4-ethanamine, 1-methyl- (9CI) (CA INDEX NAME)

Recrystn. of the dipicrate yielded only that of the 1,4-isomer, m. 216.5-17.5°; the 1,5-isomer dipicrate remained in solution Injection of 1-methyl-4-(β-aminoethyl)imidazole into mice resulted in oxidation of a major portion of the compound to 1-methylimidazole-4-acetic acid. Both compds. were determined quantitatively in urine by means of isotope dilution techniques. A study of the effect of inhibitors on this oxidation in intact mice indicated that diamine oxidase played little or no role. The enzyme involved was inhibited by a **monoamine oxidase** inhibitor.

IT **501-75-7**, Imidazole, 4-(2-aminoethyl)-1-methyl-
(preparation of)

RN 501-75-7 HCAPLUS

CN 1H-Imidazole-4-ethanamine, 1-methyl- (9CI) (CA INDEX NAME)



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File 155:MEDLINE(R) 1951-2006/Feb 15
         (c) format only 2006 Dialog
File   5:Biosis Previews(R) 1969-2006/Feb W2
         (c) 2006 BIOSIS
File  34:SciSearch(R) Cited Ref Sci 1990-2006/Feb W2
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File 144:Pascal 1973-2006/Jan W4
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File 351:Derwent WPI 1963-2006/UD,UM &UP=200611
         (c) 2006  Thomson Derwent
File 357:Derwent Biotech Res. _1982-2006/Feb W3
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Set     Items   Description
S1      72709   (MAO OR MAOA? OR MONOAMINE(2N)OXIDASE)
S2     154476   MULTIPLE(2N)SCLEROSIS
S3        133   S1 AND S2
S4        122   RD  (unique items)
S5         42   S4 NOT PY=(2006 OR 2005 OR 2004 OR 2003 OR 2002)
?
?
? T S5/3 AB/1-42

 5/AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

13661831   PMID: 11297592
  Combined treatment with corticosteroids and moclobemide favors
normalization of hypothalamo-pituitary-adrenal axis dysregulation in
relapsing-remitting multiple sclerosis : a randomized, double
blind trial.
  Then Bergh F; Kumpfel T; Grasser A; Rupprecht R; Holsboer F; Trenkwalder
C
  Department of Neurology, Max Planck Institute of Psychiatry, 80804
Munich, Germany. thenberf@ninds.nih.gov
  Journal of clinical endocrinology and metabolism (United States) Apr
2001, 86 (4) p1610-5, ISSN 0021-972X Journal Code: 0375362
  Publishing Model Print
  Document type: Clinical Trial; Journal Article; Randomized Controlled
Trial
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: MEDLINE; Completed
  Hyperresponsiveness of the hypothalamo-pituitary-adrenal (HPA) axis in
multiple sclerosis (MS), an autoimmune inflammatory disease of
the central nervous system, is presumably due to diminished corticosteroid
receptor function. It probably influences the immune response, but its
clinical significance is not clear. Similar HPA dysregulation occurs in
depression and is reversible with successful antidepressant treatment. We
conducted a double blind, placebo-controlled trial to evaluate the
neuroendocrine effect of cotreatment with the antidepressant moclobemide as
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an adjunct to oral corticosteroids in MS. Twenty-one patients with definite relapsing-remitting MS (11 females, aged 33.9 +/- 2.0 yr; Expanded Disability Status Scale score of neurological impairment, 2.0--6.5) in acute relapse were treated with placebo (n = 13) or 300 mg moclobemide (reversible **monoamine oxidase** A inhibitor; n = 8) for 75 days.
All received oral fluocortolone from day 7 on, and the dose was tapered until day 29. Effects were evaluated using the combined dexamethasone-CRH test and clinically on days 1, 30, and 75. At baseline, the HPA axis was mildly activated, comparably for treatment groups [area under the curve for cortisol (AUC-Cort), 213.8 +/- 76.8 arbitrary units in the moclobemide group vs. 225.8 +/- 65.1 in the steroid alone group; mean +/- SEM]. In a group of healthy controls with comparable demographic characteristics, the AUC-Cort was 107.4 +/- 14.1. Moclobemide cotreatment resulted in normalization of the HPA axis response, whereas the HPA system hyperresponse was maintained with steroids alone (AUC-Cort on day 30, 85.9 +/- 22.8 vs.177.1 +/- 68.5; on day 75, 111.0 +/- 46.0 vs. 199.2 +/- 64.6). The change in Expanded Disability Status Scale was comparable for both groups. Although corticosteroids alone had no effect on the HPA response using the dexamethasone-CRH test, treatment with moclobemide combined with corticosteroids favors normalization of the HPA response in relapsing-remitting MS.

5/AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13379426 PMID: 10334000
Moclobemide treatment in **multiple sclerosis** patients with comorbid depression: an open-label safety trial.
Barak Y; Ur E; Achiron A
Multiple Sclerosis Center, Sheba Medical Center, Tel-Hashomer, Israel.
Journal of neuropsychiatry and clinical neurosciences (UNITED STATES) Spring 1999, 11 (2) p271-3, ISSN 0895-0172 Journal Code: 8911344
Publishing Model Print
Document type: Clinical Trial; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Depression is common in **multiple sclerosis** (MS) patients, but tricyclic compounds are not well tolerated and newer antidepressants have not been studied. Effects of 150-400 mg/day of moclobemide, a reversible **monoamine oxidase** A inhibitor, were studied in a 3-month open design in 10 MS patient with DSM-IV-diagnosed depression. Nine patients reached complete remission. No adverse effects were noted. Four patients reported side effects including nausea and insomnia. The authors conclude that moclobemide is a well tolerated and efficient treatment for depression comorbid with MS.

5/AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10795288 PMID: 7527888
Selective **MAO** -A and B inhibitors, radical scavengers and nitric oxide synthase inhibitors in Parkinson's disease.
Youdim M B; Lavie L
Department of Pharmacology, Bruce Rappaport Faculty of Medicine, Technion, Haifa, Israel.

Life sciences (ENGLAND) 1994, 55 (25-26) p2077-82, ISSN 0024-3205
Journal Code: 0375521
Publishing Model Print
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

In the absence of identification of either an endogenously or an exogenously derived dopaminergic neurotoxin, the most valid hypothesis currently envisaged for etiopathology of Parkinson's disease (PD) is selective oxidative stress (OS) in substantia nigra (SN). Although OS is not proven, a significant body of evidence from studies on animal and Parkinsonian brain neurochemistry supports it. This hypothesis is based on excessive formation of reactive oxygen species (O2 and OH.) and demise of systems involved with scavenging or preventing the formation of such radicals from H2O2, generated as a consequence of dopamine oxidation (autoxidation and deamination). Since **MAO** (**monoamine oxidase** A and B are the major H2O2 generating enzymes in the SN much attention has been paid to their selective inhibitors as symptomatic and neuroprotective agents in PD. Attention should also be given to radical scavengers (e.g. iron chelators, lipid peroxidative inhibitors and Vitamin E derivatives) as therapeutic neuroprotective agents in PD. This is considered valid since a significant elevation of iron is known to occur selectively in SN zone compacta and within the remaining melanized dopamine neurons of Parkinsonian brains. Although all the mechanism of iron induced oxygen free radical formation is not fully known there is no doubt that it participates with H2O2 (Fenton chemistry) to generate cytotoxic hydroxyl radical (OH.) and induce tissue OS and neurodegeneration in 6-hydroxydopamine model of PD. The dramatic proliferation of reactive amoeboid macrophages and microglia seen in SN of PD brains together with OS is highly compatible with an inflammatory process, similar to what has been observed in Alzheimer's disease and **multiple sclerosis** brains.
This has led us to examine the ability of reactive macrophages to produce oxygen free radicals in response to nitric oxide (NO) production. The latter radical has been implicated in the excitotoxicity of glutaminergic neurons innervating the striatum and SN. Indeed we have now observed that in reactive macrophages NO acts as a signal transducer of O2 production which can synergize with dopamine oxidation.

5/AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09684740 PMID: 1792858
Platelet **monoamine oxidase** and plasma dopamine-beta-hydroxylase activities in patients with **multiple sclerosis**.
Markianos M; Sfagos C; Bistolaki E
Athens University Medical School, Psychiatric Clinic, Greece.
Acta neurologica Scandinavica (DENMARK) Dec 1991, 84 (6) p531-3, ISSN 0001-6314 Journal Code: 0370336
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

Platelet **monoamine oxidase** (**MAO**) and plasma dopamine-beta-hydroxylase (DBH) activities were determined in a large group of multiple sclerose patients in relapse (49 patients) and in remission (28

patients), and compared with an age- and sex-matched control group (52 normal subjects). The activities of both enzymes did not differ from normal in both patient groups. Women had higher **MAO** activities both in normal and in patient groups. Multiple linear regression analysis revealed an association of low platelet **MAO** to the score in the mental subscale in the Kurtzke Disability Status Scale. Both male and female patients with mental symptomatology had significantly ($p = 0.02$) lower platelet **MAO** activities compared to the patients without. The possibility of a relationship between **MAO** activity and psychiatric vulnerability in MS is considered.

5/AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07610931 PMID: 3088916
The management of resistant depression.
Levine S
Acta psychiatrica Belgica (BELGIUM) Mar-Apr 1986, 86 (2) p141-51, ISSN 0300-8967 Journal Code: 0247037
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Between 10 and 30% of depressed patients, mostly bipolar, develop a therapy-resistant illness. The known causes of such chronic evolutions are discussed: misdiagnosis (underlying schizophrenia, personality disorder or dementia), drug-induced depression (neuroleptics), systemic disease (hypothyroidism, **multiple sclerosis** , cardiovascular or neoplastic disease etc.), or lack of efficacy (drug compliance, insufficient dosage). Remedies are suggested: adequate dosage, drug combination (Newcastle cocktail. tricyclic antidepressant + MAOI, imipramine + T3), carbamazepine in lithium-resistant cases, alprazolam, reduction in vanadium intake, sleep deprivation, psychosurgery.

5/AB/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06161672 PMID: 6270514
A biochemical basis for the actions of lithium on behaviour and on immunity: relapsing and remitting disorders of inflammation and immunity such as **multiple sclerosis** or recurrent herpes as manic-depression of the immune system.
Horrobin D F; Lieb J
Medical hypotheses (ENGLAND) Jul 1981, 7 (7) p891-905, ISSN 0306-9877 Journal Code: 7505668
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

5/AB/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04185790 PMID: 4360370
[Disorders in the neurotransmitter system in **multiple sclerosis**?]
Storungen im Neurotransmitter-System bei multipler Sklerose.
Harrer G
Deutsche medizinische Wochenschrift (GERMANY, WEST) Oct 19 1973, 98 (42) p1988-9, ISSN 0012-0472 Journal Code: 0006723
Publishing Model Print
Document type: Journal Article
Languages: GERMAN
Main Citation Owner: NLM
Record type: MEDLINE; Completed

5/AB/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

02710506 PMID: 5243906
The side effects of carbamazepine therapy.
Redpath T H; Gayford J J
Oral surgery, oral medicine, and oral pathology (UNITED STATES) Sep 1968, 26 (3) p299-303, ISSN 0030-4220 Journal Code: 0376406
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

5/AB/9 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0013068462 BIOSIS NO.: 200100240301
Combined treatment with corticosteroids and moclobemide favors normalization of hypothalamo-pituitary-adrenal axis dysregulation in relapsing-remitting **multiple sclerosis**: A randomized, double blind trial
AUTHOR: Bergh Florian Then (Reprint); Kuempfel Tania; Grasser Annette; Rupprecht Rainer; Holsboer Florian; Trenkwalder Claudia
AUTHOR ADDRESS: Laboratory of Molecular Biology, National Institute of Neurological Diseases and Stroke, National Institutes of Health, 36 Convent Drive, Room 3C11, Bethesda, MD, 20892-4092, USA**USA
JOURNAL: Journal of Clinical Endocrinology and Metabolism 86 (4): p 1610-1615 April, 2001 2001
MEDIUM: print
ISSN: 0021-972X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Hyperresponsiveness of the hypothalamo-pituitary-adrenal (HPA) axis in **multiple sclerosis** (MS), an autoimmune inflammatory disease of the central nervous system, is presumably due to diminished corticosteroid receptor function. It probably influences the immune response, but its clinical significance is not clear. Similar HPA dysregulation occurs in depression and is reversible with successful antidepressant treatment. We conducted a double blind, placebo-controlled

trial to evaluate the neuroendocrine effect of cotreatment with the antidepressant moclobemide as an adjunct to oral corticosteroids in MS. Twenty-one patients with definite relapsing-remitting MS (11 females, aged 33.9 +- 2.0 yr; Expanded Disability Status Scale score of neurological impairment, 2.0-6.5) in acute relapse were treated with placebo (n = 13) or 300 mg moclobemide (reversible **monoamine oxidase** A inhibitor; n = 8) for 75 days. All received oral fluocortolone from day 7 on, and the dose was tapered until day 29. Effects were evaluated using the combined dexamethasone-CRH test and clinically on days 1, 30, and 75. At baseline, the HPA axis was mildly activated, comparably for treatment groups (area under the curve for cortisol (AUC-Cort), 213.8 +- 76.8 arbitrary units in the moclobemide group vs. 225.8 +- 65.1 in the steroid alone group; mean +- SEM). In a group of healthy controls with comparable demographic characteristics, the AUC-Cort was 107.4 +- 14.1. Moclobemide cotreatment resulted in normalization of the HPA axis response, whereas the HPA system hyperresponse was maintained with steroids alone (AUC-Cort on day 30, 85.9 +- 22.8 vs. 177.1 +- 68.5; on day 75, 111.0 +- 46.0 vs. 199.2 +- 64.6). The change in Expanded Disability Status Scale was comparable for both groups. Although corticosteroids alone had no effect on the HPA response using the dexamethasone-CRH test, treatment with moclobemide combined with corticosteroids favors normalization of the HPA response in relapsing-remitting MS.

5/AB/10 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0013022169 BIOSIS NO.: 200100194008
Treatment of **multiple sclerosis** (MS) and other demyelinating conditions using lofepramine in combination with L-phenylalanine, tyrosine or tryptophan and possibly a vitamin B12 compound
AUTHOR: Loder Cari (Reprint)
AUTHOR ADDRESS: 127 Russell Court, Woburn Place, London WC1H 0LP, UK**UK
JOURNAL: Official Gazette of the United States Patent and Trademark Office Patents 1237 (1): Aug. 1, 2000 2000
MEDIUM: e-file
PATENT NUMBER: US 6096737 PATENT DATE GRANTED: August 01, 2000 20000801
PATENT CLASSIFICATION: 514-217 PATENT COUNTRY: USA
ISSN: 0098-1133
DOCUMENT TYPE: Patent
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The use of a combination of a tricyclic or tetracyclic antidepressant, a serotonin reuptake inhibitor, or a **monoamine oxidase** inhibitor with a neurotransmitter-inducing or precursor compound is proposed in the preparation of medication for the treatment or prevention of **multiple sclerosis** or other demyelinating conditions. For use in treatment to ameliorate the effects of a demyelinating condition, a daily regime is proposed of from 10 to 220 mg lofepramine and from 100 mg to 5 g of L-phenylalanine, optionally supplemented with injections of vitamin B12.

5/AB/11 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

06682927 Genuine Article#: ZK332 Number of References: 28
Title: Single-blind, placebo phase-in trial of two escalating doses of selegiline in the chronic fatigue syndrome (ABSTRACT AVAILABLE)
Author(s): Natelson BH (REPRINT) ; Cheu J; Hill N; Bergen M; Korn L; Denny T; Dahl K
Corporate Source: UNIV MED & DENT NEW JERSEY,NEW JERSEY MED SCH, DEPT NEUROSCI, 88 ROSS ST/E ORANGE//NJ/07018 (REPRINT); UNIV MED & DENT NEW JERSEY,NEW JERSEY MED SCH, DEPT PEDIAT/E ORANGE//NJ/07018; UNIV MED & DENT NEW JERSEY,NEW JERSEY MED SCH, CFS CTR/E ORANGE//NJ/07018
Journal: NEUROPSYCHOBIOLOGY, 1998, V37, N3, P150-154
ISSN: 0302-282X Publication date: 19980000
Publisher: KARGER, ALLSCHWILERSTRASSE 10, CH-4009 BASEL, SWITZERLAND
Language: English Document Type: ARTICLE
Abstract: Aim: To perform a clinical trial of selegiline in 25 patients with chronic fatigue syndrome (CFS) where patients were told they would receive placebo or active agent at different times during the 6-week trial. We chose selegiline, a specific **monoamine oxidase** (**MAO**) B receptor inhibitor, because a prior trial of low-dose phenelzine, a nonspecific **MAO** inhibitor, showed a small but significant therapeutic effect. Methods: Questionnaires comprised of 19 tests of mood, fatigue, functional status and symptom severity were collected at the start and end of the trial as well as 2 weeks after its start. The trial was done in three 2-week blocks: in the first, 2 placebo pills were given per day; in the next, one 5-mg tablet of agent and one placebo were given per day, and in the last, a 5-mg tablet of agent was given twice a day. The plan was to compare the changes in the 19 tests during the placebo phase to those found in the active treatment phase in 19 patients completing the trial. Findings: Significant improvement in 3 variables - tension/anxiety, vigor and sexual relations - was found. A significant pattern of improvement compared to worsening was found for the 19 self-report vehicles during active treatment as compared with placebo treatment. Evidence for an antidepressant effect of the drug was not found. Conclusions: Selegiline has a small but significant therapeutic effect in CFS which appears independent of an antidepressant effect.

5/AB/12 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

06613972 Genuine Article#: ZE895 Number of References: 40
Title: Selegiline as immunostimulant - a novel mechanism of action? (ABSTRACT AVAILABLE)
Author(s): Muller T (REPRINT) ; Kuhn W; Kruger R; Przuntek H
Corporate Source: RUHR UNIV BOCHUM,ST JOSEF HOSP, DEPT NEUROL, GUDRUNSTR 56/D-44791 BOCHUM//GERMANY/ (REPRINT)
Journal: JOURNAL OF NEURAL TRANSMISSION-SUPPLEMENT, 1998, N52, P321-328
ISSN: 0303-6995 Publication date: 19980000
Publisher: SPRINGER VERLAG, 175 FIFTH AVE, NEW YORK, NY 10010
Language: English Document Type: ARTICLE
Abstract: In clinical studies the **MAO**-B inhibitor selegiline appears to slow the progression of neurological deficits in Parkinson's disease (PD) and the cognitive decline in Alzheimer's disease (AD). The mechanisms of action remain unclear. Several lines of evidence indicate an immune-mediated pathophysiology of PD and AD. According to animal trials, selegiline increases the survival rate of immune suppressed mice. Stimulation of the immune response to bacterial or viral infection or in chronic inflammatory processes is managed by an increased synthesis of the cytokines interleukin-1 beta (IL-1 beta) and

subsequent interleukin-6 (IL-6). Outcome of viral or bacterial infections in the brain highly correlates with levels of the cytotoxic cytokine tumor-necrosis-factor-alpha (TNF). The aim of our study was to characterize the influence of selegiline on the biosynthesis of IL-1 beta, IL-6 and TNF in human peripheral blood mononuculear cells (PBMC) fi-om healthy blood donors. After isolation and washing PBMC were cultured without and with selegiline in three different concentrations (0.01 mu mol/l, 0.001 mu mol/l, 0.0001 mu mol/l) in a humidified atmosphere (7% CO2). Then cultures were centrifuged and supernatants were collected for IL-1 beta, IL-6 and TNF ELISA-assays. Treatment of cultured PBMC with various concentrations induced an increased synthesis of IL-1 beta (ANOVA F = 9.703, p = 0.0007), IL-6 (ANOVA F = 20.648. p = 0.0001) and a reduced production of TNF (ANOVA F = 3.770, p = 0.040). These results indicate, that the influence of selegiline on the cytokine biosynthesis may also contribute to its putative neuroprotective properties.

5/AB/13 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

06327691 Genuine Article#: YH602 Number of References: 55
Title: Co-culture blood-brain barrier models and their use for pharmatoxicological screening (ABSTRACT AVAILABLE)
Author(s): Reinhardt CA (REPRINT) ; Gloor SM
Corporate Source: SWISS ALTERNAT ANIM TESTING,/CH-8614 BERTSCHIKON ZURIC//SWITZERLAND/ (REPRINT); ETH ZENTRUM,INST BIOCHEM/CH-8092 ZURICH//SWITZERLAND/
Journal: TOXICOLOGY IN VITRO, 1997, V11, N5 (OCT), P513-518
ISSN: 0887-2333 Publication date: 19971000
Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD, ENGLAND OX5 1GB
Language: English Document Type: ARTICLE
Abstract: The availability of an in vitro blood-brain barrier model would represent a powerful alternative to experimental animals in pharmacological and toxicological research. This overview collects the various current approaches to build an in vitro model of the blood-brain barrier for these purposes. Purified bovine, porcine and human brain microcapillary endothelial cells as well as several immortalized cell lines have been used to model the blood-brain barrier in vitro, partly in co-culture with astrocytes of various species, or various cell lines such as C6 glioma or N2a neuroblastoma cells. The collected data indicate that functional parameters often can be induced by soluble and membrane-bound factors in such cell systems. Relevant barrier-specific parameters are reviewed: electrical resistance, and structure and function of the multidrug resistance P-glycoprotein and the gamma-glutamyl transpeptidase. Both P-glycoprotein and gamma-glutamyl transpeptidase have great influence on the pharmacodynamics, toxicology and metabolic capacity of the blood-brain barrier (drug efflux, oxidative damage, detoxification of endotoxins, etc.). Several available in vitro models appear to be suited for pharmacotoxicological screening, if the functional parameters gamma-glutamyl transpeptidase, P-glycoprotein as well as transendothelial resistance are monitored. (C) 1997 Published by Elsevier Science Ltd.

5/AB/14 (Item 4 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

05325790 Genuine Article#: VQ435 Number of References: 102
Title: SUICIDAL-BEHAVIOR IS ATTENUATED IN PATIENTS WITH **MULTIPLE-SCLEROSIS** BY TREATMENT WITH ELECTROMAGNETIC-FIELDS (Abstract Available)
Author(s): SANDYK R
Corporate Source: POB 453/ROSLYN HTS//NY/11577; NEUROCOMMUN RES LABS INC/DANBURY//CT/06811; TOURO COLL,INST BIOMED ENGN & REHABIL SERV,DEPTNEUROSCI/DIX HILLS//NY/11746
Journal: INTERNATIONAL JOURNAL OF NEUROSCIENCE, 1996, V87, N1-2, P5-15
ISSN: 0020-7454
Language: ENGLISH Document Type: REVIEW
Abstract: A marked decrease in the levels of serotonin (5-HT) and its metabolite (5-HIAA) has been demonstrated in postmortem studies of suicide victims with various psychiatric disorders. Depression is the most common mental manifestation of **multiple sclerosis** (MS) which accounts for the high incidence of suicide in this disease. CSF 5-HIAA concentrations are reduced in MS patients and nocturnal plasma melatonin levels were found to be lower in suicidal than in nonsuicidal patients. These findings suggest that the increased risk of suicide in MS patients may be related to decreased 5-HT functions and blunted circadian melatonin secretion. Previous studies have demonstrated that extracerebral applications of pulsed electromagnetic fields (EMFs) in the picotesla range rapidly improved motor, sensory, affective and cognitive deficits in MS. Augmentation of cerebral 5-HT synthesis and resynchronization of circadian melatonin secretion has been suggested as a key mechanism by which these EMFs improved symptoms of the disease. Therefore, the prediction was made that this treatment modality would result in attenuation of suicidal behavior in MS patients. The present report concerns three women with remitting-progressive MS who exhibited suicidal behavior during the course of their illness. All patients had frequent suicidal thoughts over several years and experienced resolution of suicidal behavior within several weeks after introduction of EMFs treatment with no recurrence of symptoms during a follow-up of months to 3.5 years. These findings demonstrate that in MS pulsed applications of picotesla level EMFs improve mental depression and may reduce the risk of suicide by a mechanism involving the augmentation of 5-HT neurotransmission and resynchronization of circadian melatonin secretion.

5/AB/15 (Item 5 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

04513876 Genuine Article#: TJ327 Number of References: 39
Title: RISK OF HUMAN-IMMUNODEFICIENCY-VIRUS TYPE 1-RELATED NEUROLOGIC DISEASE IN A COHORT OF INTRAVENOUS-DRUG-USERS (Abstract Available)
Author(s): MARDER K; LIU XH; STERN Y; MALOUF R; DOONEIEF G; BELL K; TODAK G ; JOSEPH M; SORRELL S; SADR WE; WILLIAMS JBW; EHRHARDT A; STEIN Z; GORMAN J
Corporate Source: COLUMBIA UNIV,COLL PHYS & SURG,GERTRUDE H SERGIEVSKY CTR,DEPT NEUROL,630 W 168TH ST,BOX 16/NEW YORK//NY/10032; COLUMBIA UNIV,COLL PHYS & SURG,GERTRUDE H SERGIEVSKY CTR,DEPT PSYCHIAT/NEW YORK//NY/10032; COLUMBIA UNIV,COLL PHYS & SURG,HIV CTR CLIN & BEHAV STUDIES/NEW YORK//NY/10032; COLUMBIA UNIV,SCH PUBL HLTH,DIV EPIDEMIOL/NEW YORK//NY/10032; ST LUKES ROOSEVELT HOSP/NEW YORK//NY/00000; HARLEM HOSP MED CTR/NEW YORK//NY/00000
Journal: ARCHIVES OF NEUROLOGY, 1995, V52, N12 (DEC), P1174-1182

ISSN: 0003-9942
Language: ENGLISH Document Type: ARTICLE
Abstract: Background: Although the proportion of cases of acquired immunodeficiency syndrome related to intravenous drug use has increased dramatically over the past decade, there has been no longitudinal examination of primary neurologic disease in this group.

Objective: To study the development of neurologic disease in human immunodeficiency virus (HIV)-negative and HIV-positive men and women who were intravenous drug users over a 3.5-year period.

Design: Prospective observational cohort study.

Setting: Subjects were recruited from an infectious disease clinic at a New York City Hospital or from a methadone maintenance program.

Participants: Ninety-nine HIV-negative (62 men and 37 women) and 1.24 HIV-positive (85 men and 39 women) intravenous drug users volunteered.

Main Outcome Measure: The development of clinically significant manifestations in six neurologic domains.

Results: With multivariate adjustment for current and past substance abuse, age, education, and head injury, we examined the odds of developing HIV-related neurologic disease. Extrapyramidal signs and reduced motor ability became increasingly apparent over time in HIV-infected men as their CD4 cell count declined and as the subjects developed the acquired immunodeficiency syndrome. Fewer neurologic signs were seen in the women.

Conclusions: The impact of HIV infection among intravenous drug users parallels that in homosexual men and is independent of alcohol and other drug use.

5/AB/16 (Item 6 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

04381469 Genuine Article#: RZ513 Number of References: 18
Title: NUCLEAR MICROSCOPY IN PARKINSONS-DISEASE (Abstract Available)
Author(s): WATT F; LEE T; THONG PSP; TANG SM
Corporate Source: NATL UNIV SINGAPORE,DEPT PHYS,NUCL MICROSCOPY LAB,KENT RIDGE/SINGAPORE 0511//SINGAPORE/; NATL UNIV SINGAPORE HOSP,DEPT SURG/SINGAPORE 0511//SINGAPORE/
Journal: NUCLEAR INSTRUMENTS & METHODS IN PHYSICS RESEARCH SECTION B-BEAM INTERACTIONS WITH MATERIALS AND ATOMS, 1995, V104, N1-4 (SEP), P361-364
ISSN: 0168-583X
Language: ENGLISH Document Type: ARTICLE
Abstract: Rats have been subjected to unilateral lesioning with the selective neurotoxin 6-OHDA in order to induce Parkinsonism. Analysis using the NUS Nuclear Microscope facility have shown that iron levels are raised by an average of 26% in the lesioned substantia nigra region of the brain compared with the non-lesioned side. In addition the background tissue level of iron is also elevated by 31% in the lesioned side, indicating that there is a general increase in iron levels as a result of the lesioning. This result is consistent with the other observations that other diseases of the brain are frequently associated with altered iron levels (eg. progressive nuclear palsy, multiple system atrophy, Alzheimers disease, **multiple sclerosis**).

5/AB/17 (Item 7 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

04234417 Genuine Article#: RQ231 Number of References: 88
Title: PSYCHOSES IN **MULTIPLE-SCLEROSIS** - A REASSESSMENT (Abstract Available)
Author(s): SCHIFFERDECKER M; KRAHL A; KREKEL NO
Corporate Source: UNIV COLOGNE,NEUROL & PSYCHIAT KLIN & POLIKLIN,JOSEPH STELZMANN STR 9/D-50924 COLOGNE//GERMANY/
Journal: FORTSCHRITTE DER NEUROLOGIE PSYCHIATRIE, 1995, V63, N8 (AUG), P 310-319
ISSN: 0720-4299
Language: GERMAN Document Type: ARTICLE
Abstract: With the aim of reaching a new classification of psychoses with **multiple sclerosis** we reviewed the twentieth century literatur for observations with regard to the subject, as well as 688 medical records of our patients, looking for the occurrence of paranoid and hallucinatory psychoses in the course of **multiple sclerosis**. Special attention was paid to the occurrence of cycloid psychoses.

With **multiple sclerosis**, psychoses on the whole - but cycloid psychoses in particular - occur more frequently than in the general population. Women are affected just as frequently as men. Cycloid psychoses occur earlier in the course of the **multiple sclerosis** than the other psychoses; here, hallucinations occur with a higher frequency.

Similar as in the case of HIV-infection, **multiple sclerosis** can act as a trigger of a cycloid psychosis. The results of our study indicate that men and women experience this disease as similarly threatening. A shortcoming of critical faculties based on the organic disease is an additional factor that favours the outbreak of such a psychosis.

5/AB/18 (Item 8 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

04144629 Genuine Article#: RH641 Number of References: 79
Title: IRON IN CNS DISEASE
Author(s): GELMAN BB
Corporate Source: UNIV TEXAS,MED BRANCH,DEPT PATHOL,G-85/GALVESTON//TX/77550
Journal: JOURNAL OF NEUROPATHOLOGY AND EXPERIMENTAL NEUROLOGY, 1995, V54, N4 (JUL), P477-486
ISSN: 0022-3069
Language: ENGLISH Document Type: REVIEW

5/AB/19 (Item 9 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

03952503 Genuine Article#: QV058 Number of References: 42
Title: LOCALIZED PROTON NMR-SPECTROSCOPY IN THE STRIATUM OF PATIENTS WITH

IDIOPATHIC PARKINSONS-DISEASE - A MULTICENTER PILOT-STUDY (Abstract Available)
Author(s): HOLSHOUSER BA; KOMU M; MOLLER HE; ZIJLMANS T; KOLEM H; HINSHAW DB; SONNINEN P; VERMATHEN P; HEERSCHAP A; MASUR H; RINNE UK; DEKOSTER A ; TOSK JM
Corporate Source: JERRY L PETTIS MEM VET ADM MED CTR,PARKINSONS RES CTR,PSYCHIAT SERV 116A,11202 BENTON ST/LOMA LINDA//CA/92357; JERRY L PETTIS MEM VET ADM MED CTR,PARKINSONS RES CTR,PSYCHIAT SERV 116A/LOMA LINDA//CA/92357; LOMA LINDA UNIV,SCH MED,DEPT RADIOL/LOMA LINDA//CA/00000; LOMA LINDA UNIV,SCH MED,DEPT NEUROL/LOMA LINDA//CA/00000; LOMA LINDA UNIV,SCH MED,DEPT PSYCHIAT/LOMA LINDA//CA/00000; LOMA LINDA UNIV,SCH MED,DEPT PHYSIOL/LOMA LINDA//CA/00000; LOMA LINDA UNIV,SCH MED,PARKINSONS RES CTR/LOMALINDA//CA/00000; UNIV CENT HOSP,DEPT RADIOL/TURKU//FINLAND/; UNIV CENT HOSP,NEUROL CLIN/TURKU//FINLAND/; UNIV MUNSTER,INST PHYS CHEM/MUNSTER//GERMANY/; UNIV MUNSTER,NEUROL KLIN & POLIKLIN/MUNSTER//GERMANY/; UNIV NIJMEGEN HOSP,DEPT NEUROL/NIJMEGEN//NETHERLANDS/; UNIV NIJMEGEN HOSP,DEPT DIAGNOST RADIOL/NIJMEGEN//NETHERLANDS/; SIEMENS AG,MED ENGN GRP/ERLANGEN//GERMANY/
Journal: MAGNETIC RESONANCE IN MEDICINE, 1995, V33, N5 (MAY), P589-594
ISSN: 0740-3194
Language: ENGLISH Document Type: ARTICLE
Abstract: Single voxel proton MRS was used to study brain metabolism in the striatum of patients diagnosed with idiopathic Parkinson's disease (PD). Peak metabolite ratios in long echo time spectra were evaluated in 151 patient spectra and 97 age-matched control spectra collected at four participating institutions using identical hardware and clinical protocols. Combining data from all ages (27-83 years old) showed no significant difference between patient and control ratios. However, in an elderly subset of patients (51-70 years old), a significant decrease in striatal N-acetylaspartate (NAA)/choline (Cho) was observed. Also, a significant decrease in the mean NAA/Cho ratio was observed in patients versus controls for patients not being treated with Sinemet (Du Pont Pharm, Wilmington, DE) (hereafter referred to as levodopa/carbidopa). This result is consistent with the hypothesis that NAA may provide a reversible spectroscopic marker for neuronal dysfunction, although a prospective follow-up study will be needed to confirm this. Quantitation of MRS would be useful to exclude the possibility that a change in Cho levels affected the NAA/Cho ratios.

5/AB/20 (Item 10 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

03813936 Genuine Article#: QG820 Number of References: 52
Title: BRAIN REPAIR (Abstract Available)
Author(s): COMPSTON A
Corporate Source: UNIV CAMBRIDGE,ADDENBROOKES HOSP,NEUROBIOL UNIT,NEUROL UNIT,HILLS RD/CAMBRIDGE CB2 2QQ//ENGLAND/; MRC,CAMBRIDGE CTR BRAIN REPAIR/CAMBRIDGE//ENGLAND/
Journal: JOURNAL OF INTERNAL MEDICINE, 1995, V237, N2 (FEB), P127-134
ISSN: 0954-6820
Language: ENGLISH Document Type: REVIEW
Abstract: Significant improvements in the treatment of common neurological diseases can be expected over the next few years from the application of advances now occurring in the basic neuroscience. In many disorders of the central nervous system, disability accumulates as a result of the degenerative process and its failure to repair. In part, this is

because with differentiation, cells in the adult nervous system lose the ability to proliferate an migrate. A family of growth factors orchestrates proliferation, migration, differentiation and survival of neurones and glia; because certain of these growth factors also protect from injury cells which they support during development, there should soon be opportunities for limiting damage following a variety of insults and for rescuing degenerating neurones and glia. The discovery that axon regeneration is actively inhibited, perhaps in order to maintain stability in the complex systems and circuits that are established during development, suggests new strategies for enhancing axonal regeneration in spinal and head injury. Recruiting cells that are capable of restoring glial-neuronal interactions into areas of damage will be an important part of the brain repair strategy but it may prove possible to restore complex cellular arrangements through cell implantation only. Grafted neurones survive, produce appropriate neurotransmitters, form connections and restore some behaviours, but their relative inability to grow limits the degree of structural and functional repair that can be achieved; nevertheless, nerve cell implantation is now being used in the management of certain neurodegenerative diseases of the human central nervous system. There are also prospects for increasing the remyelination which occurs following acute inflammatory disease of the central nervous system, through the combination of immunological treatments that limit the disease process, growth factors that recruit oligodendrocytes and implantation of glial progenitors into demyelinated areas.

5/AB/21 (Item 11 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

03644954 Genuine Article#: PU540 Number of References: 31
Title: SELECTIVE **MAO**-A AND **MAO**-B INHIBITORS, RADICAL SCAVENGERS AND NITRIC-OXIDE SYNTHASE INHIBITORS IN PARKINSONS-DISEASE (Abstract Available)
Author(s): YOUDIM MBH; LAVIE L
Corporate Source: TECHNION ISRAEL INST TECHNOL,BRUCE RAPPAPORT FAC MED,DEPT PHARMACOL,POB 9649/IL-31096 HAIFA//ISRAEL/; TECHNION ISRAEL INST TECHNOL,BRUCE RAPPAPORT FAC MED,DEPT ANAT/IL-31096 HAIFA//ISRAEL/
Journal: LIFE SCIENCES, 1994, V55, N25-2, P2077-2082
ISSN: 0024-3205
Language: ENGLISH Document Type: ARTICLE
Abstract: In the absence of identification of either an endogenously or an exogenously derived dopaminergic neurotoxin, the most valid hypothesis currently envisaged for etiopathology of Parkinson's disease (PD) is selective oxidative stress (OS) in substantia nigra (SN). Although OS is not proven, a significant body of evidence from studies on animal and Parkinsonian brain neurochemistry supports it. This hypothesis is based on excessive formation of reactive oxygen species (O-2(.) and OH.) and demise of systems involved with scavenging or preventing the formation of such radicals from H2O2, generated as a consequence of dopamine oxidation (autoxidation and deamination). Since **MAO** (**monoamine oxidase** A and B are the major H2O2 generating enzymes in the SN) much attention has been paid to their selective inhibitors as symptomatic and neuroprotective agents in PD. Attention should also be given to radical scavengers (e.g. iron chelators, lipid peroxidative inhibitors and Vitamin E derivatives) as therapeutic neuroprotective agents in PD. This is considered valid since a significant elevation of iron is known to occur selectively in SN zone compacta and within the remaining melanized dopamine neurons of

Parkinsonian brains. Although all the mechanism of iron induced oxygen free radical formation is not fully known there is no doubt that it participates with H2O2 (Fenton chemistry) to generate cytotoxic hydroxyl radical (OH.) and induce tissue OS and neurodegeneration in 6-hydroxydopamine model of PD. The dramatic proliferation of reactive amoeboid macrophages and microglia seen in SN of PD brains together with OS is highly compatible with an inflammatory process, similar to what has been observed in Alzheimer's disease and **multiple sclerosis** brains. This has led us to examine the ability of reactive macrophages to produce oxygen free radicals in response to nitric oxide (NO) production. The latter radical has been implicated in the excitotoxicity of glutaminergic neurons innervating the striatum and SN. Indeed we have now observed that in reactive macrophages NO acts as a signal transducer of O-2(.) production which can synergize with dopamine oxidation.

5/AB/22 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

11194577 EMBASE No: 2001204102
Depression in patient with neurological disorders. Suggested schemes of treatment
DEPRESION EN PACIENTES CON PATOLOGIA NEUROLOGICA. PROPUESTA DE ESQUEMAS TERAPEUTICOS
Abreu de la Torre C.; Suarez-Monteagudo C.; Araujo-Suarez F.
Dr. C. Abreu de la Torre, Ave. 25, N. 15805 La Habana Cuba
Revista de Neurologia (REV. NEUROL.) (Spain) 16 FEB 2001, 32/4 (393-395)
CODEN: RVNRA ISSN: 0210-0010
DOCUMENT TYPE: Journal ; Article
LANGUAGE: SPANISH
NUMBER OF REFERENCES: 21

5/AB/23 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

10918080 EMBASE No: 2000412173
Pharmacological frontiers in the treatment of AIDS dementia
McGuire D.; Marder K.
D. McGuire, 643 Bair Island Road Suite 210, Redwood City, CA United States
AUTHOR EMAIL: dmcguire@csfluids.com
Journal of Psychopharmacology (J. PSYCHOPHARMACOL.) (United Kingdom) 2000, 14/3 (251-257)
CODEN: JOPSE ISSN: 0269-8811
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 46

Even in the era of highly active antiretroviral therapy, AIDS dementia remains an important and devastating complication of human immunodeficiency virus (HIV-1) infection. Based on the 1997 AIDS case rate of 56 per 100 000 population in the USA, a reasonable estimated incidence of AIDS dementia is 3-8 per 100 000, similar to that of **multiple sclerosis**. The pharmacology of AIDS dementia has been dominated by antiretroviral therapies, the best studied of which is azidothymidine. New and specific

therapies are needed to treat and prevent brain injury in the setting of HIV infection. Rational therapy has been limited by the absence of large, adequate and well-controlled clinical trials using neuroprotective agents or those with disease-modifying potential, as well as by an incomplete understanding of the pathophysiology of AIDS dementia. In this review, a summary of evidence-based hypotheses of HIV-associated brain injury is followed by information on current nonantiretroviral therapeutic trials and their scientific rationale.

5/AB/24 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE

10903783 EMBASE No: 2000387376
Multiple sclerosis, disease modifying treatments and depression: A critical methodological review
Feinstein A.
A. Feinstein, Sunnybrook and Women's College, Health Science Centre, Department of Psychiatry, 2075 Bayview Avenue, Toronto, Ont. M4N 3M5 Canada
Multiple Sclerosis (MULT. SCLER.) (United Kingdom) 2000, 6/5 (343-348)
CODEN: MUSCF ISSN: 1352-4585
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 52

Background: Major depression affects one in two patients with **multiple sclerosis** (MS) during the course of their lifetime. This adds to the morbidity associated with the disorder and may contribute to an increased mortality rate because of suicide. Over the past few years, with the advent of disease modifying treatments for MS, a new concern with respect to mood has arisen, namely the possibility that some of these drugs may have depression as a clinically significant side effect. Objective: To ascertain whether disease modifying treatments in MS are associated with the development of depression or the worsening of a depressive illness. Methodology: A MEDLINE and PSYCHLIT search focusing on depression and disease modifying treatments going back to 1993 (the publication date of the results of the first randomised, placebo controlled trial). The methodology pertaining to the assessment of depression is critically reviewed. Furthermore, a critical summary is provided of treatment modalities for the depressed MS patient. Results: There are conflicting data that depression may occur with some disease modifying drugs, particularly interferon beta-1b. However, all studies reveal limitations with respect to the assessment of mood. Some reports, despite omitting details of how mentation was assessed, still comment on the presence or absence of depression. Others suffer from one or more of the following shortcomings: a failure to assess premorbid risk factors for mood disorder; a reliance on one question to assess depression; the utilisation of self report mood rating scales of questionable validity; neglecting to distinguish depression as a symptom from depression as a syndrome (i.e. major depression as defined by the DMS-IV). Conclusions: Given the many methodological pitfalls inherent in all studies to date, it is premature to conclude that disease modifying drugs are associated with depression. Evidence suggests that treatment of depression, irrespective of a putative association with a disease modifying agent, is frequently effective. This applies to pharmacotherapy or psychotherapy, although the former may be preferred should depression arise during a course of treatment with a disease modifying agent.

5/AB/25 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE

07892772 EMBASE No: 1999366486
Medical treatment of patients with chronic psychiatric and chronic neurologic diseases in Rhineland-Palatinate
MEDIZINISCHE BEHANDLUNG FUR PATIENTEN MIT CHRONISCH PSYCHIATRISCHEN UND CHRONISCH NEUROLOGISCHEN ERKRANKUNGEN IN RHEINLAND-PFALZ
Reuther P.; Smolenski C.
Neurologie und Rehabilitation (NEUROL. REHABIL.) (Germany) 1999, 5/4 (229-232)
CODEN: NEREF ISSN: 0947-2177
DOCUMENT TYPE: Journal; Note
LANGUAGE: GERMAN

5/AB/26 (Item 5 from file: 73)
DIALOG(R)File 73:EMBASE

07667055 EMBASE No: 1999150723
Possible use of amantadine in depression
Huber T.J.; Dietrich D.E.; Emrich H.M.
Dr. T.J. Huber, Klinik fur Klinische Psychiatrie, Medizinische Hochschule Hannover, Carl-Neuberg-Strasse 1, D-30625 Hanover Germany
Pharmacopsychiatry (PHARMACOPSYCHIATRY) (Germany) 1999, 32/2 (47-55)
CODEN: PHRME ISSN: 0176-3679
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 102

Amantadine, originally used in the treatment and prophylaxis of influenza infection, has also proved beneficial in drug-induced Parkinsonism, Parkinson's disease, traumatic head injury, dementia, **multiple sclerosis** and cocaine withdrawal. Amantadine appears to act through several pharmacological mechanisms, none of which has been identified as the one chief mode of action. It is a dopaminergic, noradrenergic and serotonergic substance, blocks monoaminoxidase A and NMDA receptors, and seems to raise beta- endorphin/beta-lipotropin levels. However, it is still uncertain which of these actions are relevant in therapeutic doses. One new aspect is the antiviral effect of amantadine on Borna disease virus, which it is suspected may possibly play a role in affective disorders. All of these actions could constitute an antidepressant property, and it is suggested that amantadine might work as an antidepressant not through one, but through several mechanisms thought to be related to antidepressant activity. Effects of amantadine on symptoms of affective disorders have been demonstrated in several trials administering it for varying purposes. Additionally, animal studies as well as clinical trials in humans have hinted at an antidepressant activity of amantadine. We present here an overview of the current data. However, only a limited body of evidence is available, and further studies are needed to investigate the efficacy of amantadine as well as its modes of action in depression.

5/AB/27 (Item 6 from file: 73)
DIALOG(R)File 73:EMBASE

07131460 EMBASE No: 1998019436
Obstetric issues in women with neurologic diseases
Norwitz E.R.; Repke J.T.
Dr. E.R. Norwitz, Department of Obstetrics/Gynecology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA United States
Current Problems in Obstetrics, Gynecology and Fertility (CURR. PROBL. OBSTET. GYNECOL. FERTIL.) (United States) 1997, 20/6 (190-230)
CODEN: CPOIE ISSN: 8756-0410
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 279

During pregnancy, the investigation and management of neurologic conditions is complicated by concern about the safety of the fetus. This manuscript is designed as a clinical reference for the practicing obstetrician. It will focus on the management of late pregnancy, labor, and delivery in patients with specific neurologic ailments. A systematic, anatomic approach has been taken. The review starts with a discussion of neurologic diseases of the brain and works its way down the spinal cord and peripheral nerves, across the neuromuscular junctions to the muscles. Movement disorders are considered separately. The monograph concludes with discussions of neurologic emergencies during pregnancy, as well as other situations specific to obstetric practice (such as drugs and breast-feeding, genetic counseling, and antenatal diagnosis for inherited neurologic diseases.) Disorders of the Brain includes discussions about the incidence, differential diagnosis, and management of a number of clinical conditions that center on the brain. These include headache; seizure disorders (focusing on management issues during pregnancy and implications for the fetus and newborn); cerebrovascular disease (stroke, Sheehan's syndrome, hypertensive encephalopathy); and demyelinating and degenerating diseases (**multiple sclerosis**, Huntington's disease). Infections of the nervous system (syphilis, polio, tetanus, toxoplasmosis, Lyme disease, HIV) occur in pregnancy, as they do in the nonpregnant state, but diagnosis and management might be different. The effects of inflammatory conditions of the central nervous system and intracranial tumors on pregnancy are reviewed briefly. There is a separate discussion about radiation exposure and its effects on the developing fetus. This discussion concludes that, in general, the use of radiographic technology (either diagnostic or therapeutic), if indicated, should not be restricted because the patient is pregnant. Psychiatric disorders affecting pregnancy (those that precede pregnancy, as well as conditions that result from pregnancy-such as postpartum depression and psychosis) often are overlooked. The warning signs and treatment of such conditions are discussed in detail. Disorders of the Spinal Cord includes discussions about specific topics (such as pregnancy in women with spinal-cord injuries and the entity of autonomic dysreflexia), as well as some more general topics (such as backache in pregnancy). Disorders of Peripheral Nerves covers both mononeuropathies (carpal tunnel syndrome, Bell's palsy, meralgia paresthetica) and polyneuropathies (Guillain-Barre syndrome, porphyric neuropathy, and the hereditary polyneuropathies). The 'lithotomy' position derives its name from Greek 'lithos,' meaning stone, and 'otomy,' meaning to cut. It is so named because it was the position in which elderly men were placed for surgical removal of obstructing bladder stones. It is not a natural position for childbirth and might create nerve injury as the result of compression and/or stretching of a particular peripheral nerve of nerve plexus. Symptoms of such obstetric neuropathies are usually mild and unilateral, and complete recovery can be expected in the majority of cases. These are reviewed in greater detail. Disorders of the Neuromuscular Junction focuses on myasthenia gravis, its effect on pregnancy, implications for the fetus and newborn, and management during labor and

delivery. Disorders of Muscle includes brief discussions about muscle cramping and a number of specific muscular disorders, such as myotonic dystrophy, myotonia congenita, and polymyositis/dermatomyositis. Movement disorders are considered separately. These include a definition of some of the generalized involuntary movements, with specific reference to chorea gravidarum and Wilson's disease. Localized involuntary movements are discussed briefly, including the 'restless leg syndrome,' which is reputed to be the most common movement disorder in pregnancy. It usually occurs in the third trimester and has been reported in up to 11% to 12% of all pregnancies. Neurologic Emergencies During Pregnancy reviews the management of such conditions as status epilepticus and disorders of consciousness (coma) during pregnancy and delivery. Miscellaneous Neurologic Conditions Specific to Pregnancy includes such topics as neurologic birth injury (intracranial hemorrhage, brachial- plexus injury, fetal acidosis, cerebral palsy) and other congenital neurologic injuries (facial nerve paralysis, injuries to the neck and spine, multicystic encephalomalacia). Many factors might put a fetus at risk for a genetic disorder or neurologic birth defect. The section Neurologic Disorders in the Fetus explores the need for comprehensive genetic counseling both before and after conception. A number of preventative measures are outlined. They might ameliorate the risk of congenital neurologic anomaly, such as meticulous periconceptional glucose control in women with insulin-dependent diabetes, folic acid supplementation for women who have had a previous fetus with neural-tube defect, and parental karyotyping for couples at risk of having a fetus with one of the more common autosomal recessive disorders (Tay-Sachs disease, cystic fibrosis, sickle cell anemia). Recommendations for routine prenatal screening (including maternal serum alpha-fetoprotein, triple-panel serum screening, ultrasonography, and amniocentesis and other fetal genetic testing) are reviewed in detail. The section ends with a detailed discussion on drugs and breast-feeding. In general, most chronic neurologic disorders are compatible with normal pregnancy outcome. Diagnostic investigations (including imaging studies) and treatment protocols should be initiated, if indicated. The implications of such interventions for the developing fetus, however, should not be overlooked.

5/AB/28 (Item 7 from file: 73)
DIALOG(R)File 73:EMBASE

06130885 EMBASE No: 1995162262
Medical use of psychostimulants: An overview
Holmes V.F.
DUMC 3335,Durham, NC 27710 United States
International Journal of Psychiatry in Medicine (INT. J. PSYCHIATRY MED.) (United States) 1995, 25/1 (1-19)
CODEN: IJMED ISSN: 0091-2174
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

This overview addresses the basic chemistry, pharmacology, activity, medical uses, drug interactions and adverse side effects of the psychostimulants.

5/AB/29 (Item 8 from file: 73)
DIALOG(R)File 73:EMBASE

05699453 EMBASE No: 1994104417

Various forms of tremor: How to identify them and how to treat them?
VERSCHIEDENE TREMORFORMEN. WIE ERKENNEN, WIE BEHANDELN?
Aschoff J.C.
Abteilung Neurologie, Universitat Ulm, Steinhovelstrasse 9,88075 Ulm Germany
Therapiewoche (THERAPIEWOCHE) (Germany) 1994, 44/10 (586-591)
CODEN: THEWA ISSN: 0040-5973
DOCUMENT TYPE: Journal; Review
LANGUAGE: GERMAN SUMMARY LANGUAGE: GERMAN; ENGLISH

Tremors are mainly differentiated into resting tremor and tremor of posture and action. All the subtypes including physiological, drug induced and psychogenic tremor are diagnosed by observation of the tremor habitat in its predominant occurrence. Betablockers dominate in the treatment of benign essential tremor (with its familial and senile varieties). The efficacy of anti-Parkinson drugs is yet unsatisfactory with respect to tremor reduction. Intention-tremor due to cerebellar lesions can be efficiently treated neither by drugs nor by neurosurgical procedures.

5/AB/30 (Item 9 from file: 73)
DIALOG(R)File 73:EMBASE

05530852 EMBASE No: 1993298951
Neurodegenerative disorders: Patent activity between January and June 1993
Jaen J.C.
Parke-Davis Pharmaceutical Res Div, Warner-Lambert Company, 2800 Plymouth Road,Ann Arbor, MI 48105 United States
Current Opinion in Therapeutic Patents (CURR. OPIN. THER. PAT.) (United Kingdom) 1993, 3/9 (1335-1346)
CODEN: COTPE ISSN: 0962-2594
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH

5/AB/31 (Item 10 from file: 73)
DIALOG(R)File 73:EMBASE

02052523 EMBASE No: 1982217617
Drug treatment in **multiple sclerosis**
Kelly R.
Dept. Neurol., St Thomas' Hosp., London United Kingdom
Physiotherapy (PHYSIOTHERAPY) (United Kingdom) 1982, 68/5 (146-148)
CODEN: PHSIA
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

5/AB/32 (Item 11 from file: 73)
DIALOG(R)File 73:EMBASE

01798334 EMBASE No: 1981233287
Adrenergic influences on spasticity. Studies on the influences of alpha- and beta-adrenergic blockade on proprioceptive reflexparameters in spastic patients
Mai J.

Denmark
Acta Neurologica Scandinavica (ACTA NEUROL. SCAND.) (Denmark) 1981, 63/Suppl. 85 (1-143)
CODEN: ANRSA
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH SUMMARY LANGUAGE: DANISH

The present study is a neurophysiological investigation into the mode of action of alpha- and beta-adrenergic blockade on proprioceptive reflex activity - and thus on spasticity. The study has been conducted exclusively on humans, mainly patients suffering from **multiple sclerosis** and spasticity.

5/AB/33 (Item 12 from file: 73)
DIALOG(R)File 73:EMBASE

01333864 EMBASE No: 1979054523
Attacks of acute headache
LES EPISODES DE CEPHALEES AIGUES
Aimard G.; Trouillas P.
Hop. Neurol., 69394 Lyon Cedex 3 France
Semaine des Hopitaux (SEM. HOP.) (France) 1978, 54/33-36 (1059-1061)
CODEN: SHPAA
DOCUMENT TYPE: Journal
LANGUAGE: FRENCH SUMMARY LANGUAGE: ENGLISH

Acute headaches are in most cases significant symptoms or premonitory signs of a neurological condition. From a semiological point of view, they may be : (i) isolated, (ii) associated with neurological symptoms (ophthalmoplegia, hemiplegia, hemianesthesia). From an etiological point of view, the haemorrhagic conditions are predominant (30 %) : encephalic vascular malformation with or without subarachnoidal haemorrhagia (21 %), subarachnoidal haemorrhagia without malformation (6%) and subdural haematoma (3%). Two types of conditions are also frequently observed : ischemic attacks (22,3 %) and inflammatory meningeal syndromes (12 %). Rare cases with hypophyseal adenomas, ischemic attacks under oestro-progestative treatment, accidents of mono-amine-oxydase inhibitors and **multiple sclerosis** are observed. 23,8 % of the cases remained without any precise diagnosis. One of the interesting points in the acute headache issue is the possibility of discovering an encephalic vascular malformation without any important bleeding and, therefore, good conditions for surgery.

5/AB/34 (Item 13 from file: 73)
DIALOG(R)File 73:EMBASE

01122751 EMBASE No: 1978252934
Clinical, biochemical, and physiological features distinguishing myoclonus responsive to 5 hydroxytryptophan, tryptophan with a **monoamine oxidase** inhibitor, and clonazepam
Chadwick D.; Hallett M.; Harris R.; et al.
University Dept. Neurol., Inst. Psychiat., London United Kingdom
Brain (BRAIN) (United Kingdom) 1977, 100/3 (455-487)
CODEN: BRAIA
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

Fifteen patients with a variety of myoclonic syndromes were studied clinically, pharmacologically, and physiologically. CSF tryptophan, 5HIAA, and HVA were also measured. Of these patients, 8 were improved to varying degrees by therapy with 5HTP, tryptophan in combination with MAOI (but not tryptophan alone), and clonazepam. This group included 6 cases of post-anoxic myoclonus, 1 case of post-traumatic myoclonus and 1 undiagnosed case of non-progressive focal myoclonus and epilepsy. In this group low levels of CSF 5HIAA were found compared to non-responsive cases and controls. Two cases of dyssynergia cerebellaris myoclonica, 2 cases of undiagnosed etiology, 2 cases of essential myoclonus, and 1 case of palatal myoclonus failed to respond to drug therapy. However, even amongst the responsive group the improvement varied. The most dramatic responses were seen in those patients in whom physiological study suggested that myoclonus was mediated by brain-stem structures. Less dramatic responses were seen in patients in whom the myoclonus appeared to originate from cortical structures. The neurochemical basis of myoclonus responding to 5HT precursors and clonazepam is discussed. It is suggested that such myoclonus arises from a relative hypoactivity of the 5HT neuronal system which results in a release of abnormal responses to sensory stimuli which characterize this type of myoclonus.

5/AB/35 (Item 14 from file: 73)
DIALOG(R)File 73:EMBASE

00944552 EMBASE No: 1978072861
Catecholamines in the central nervous system. Physiologic and pathologic survey
LES CATECHOLAMINES DU SYSTEME NERVEUX CENTRAL. APERCU PHYSIOLOGIQUE ET PATHOLOGIQUE
Rascol A.; Guiraud B.; David J.; Montastruc J.L.
Serv. Neurol., CHU Purpan, Toulouse France
Revue de Medecine de Toulouse (REV. MED. TOULOUSE) (France) 1977, 13/3 sup (231-240)
CODEN: RMDTA
DOCUMENT TYPE: Journal
LANGUAGE: FRENCH

5/AB/36 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal

10022341 PASCAL Number: 92-0114754
Platelet **monoamine oxidase** and plasma dopamine-beta-hydroxylase activities in patients with multiple slerosis
MARKIANOS M; SFAGOS C; BISTOLAKI E
Athens university medical school, psychiatric clin., Athens, Greece
Journal: Acta neurologica scandinavica, 1991, 84 (6) 531-533
Language: English Summary Language: English
Platelet **monoamine oxidase** (**MAO**) and plasma dopamine-beta -hydroxylase (DBH) activities were determined in a large group of multiple sclerose patients in relapse (49 patients) and in remission (28 patients), and compared with an age- and sex-matched control group (52 normal subjects). The activities of both enzymes did not differ from normal in both patient groups. Women had higher **MAO** activities both in normal and in patient groups. Multiple linear regression analysis revealed an association of low platelet **MAO** to the score in the mental subscale in the Kurtzke Disability Status Scale

5/AB/37 (Item 1 from file: 351)
DIALOG(R)File 351:Derwent WPI

013157209
WPI Acc No: 2000-329082/200028
XRAM Acc No: C00-099736
Treatment of neurodegeneration using compounds which inhibit p25 accumulation, useful for treating e.g. Alzheimer's disease, Down's syndrome, Parkinson's disease, Huntington's disease, **multiple sclerosis** or dementia
Patent Assignee: HARVARD COLLEGE (HARD)
Inventor: LEE M S; PATRICK G N; TSAI L
Number of Countries: 020 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200021550	A2	20000420	WO 99US24221	A	19991013	200028	B

Priority Applications (No Type Date): US 99136631 P 19990527; US 98103975 P 19981013
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200021550	A2	E	53	A61K-038/00	

Designated States (National): CA JP
Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

Abstract (Basic): WO 200021550 A2
Abstract (Basic):

NOVELTY - New methods for treating or preventing neurodegenerative disease (ND) comprise administering compounds which inhibit accumulation of p25.

DETAILED DESCRIPTION - A novel method of preventing or treating a ND in an individual comprises administering one or more compounds that reduce conversion of p35 to p25 in neurological tissue.

INDEPENDENT CLAIMS are also included for:

(1) a method of preventing or treating a ND in an individual which is associated with neurofibrillatory tangles and accumulation of p25 in neurological tissue, comprising administering to the individual compounds that inhibit deregulation of a cdk5 kinase;

(2) a method of preventing or treating a ND in an individual which is associated with neurofibrillatory tangles and accumulation of p25 in neurological tissue, comprising administering one or more compounds that reduce phosphorylation of tau by a p25/cdk5 kinase;

(3) a method of treating a ND in an individual which is associated with neurofibrillatory tangles and accumulation of p25 in the brain, comprising administering to the individual one or more compounds that reduce accumulation of p25 in the brain;

(4) a method of preventing or treating a ND in an individual comprising administering one or more calpain inhibitors or antagonists which reduce conversion of p35 to p25;

(5) a method of preventing or treating a ND in an individual comprising administering one or more cation antagonists or inhibitors which reduce conversion of p35 to p25;

(6) a method of inhibiting or reducing conversion of p35 to p25 in neuronal tissue comprising contacting one or more calpain inhibitors or antagonists, and/or one or more cation inhibitors or antagonists with the neuronal tissue;

(7) a method of preventing or reducing neurofibrillatory tangles comprising contacting one or more calpain inhibitors or antagonists, and/or one or more cation inhibitors or antagonists with neuronal tissue, whereby conversion of p35 to p25 is reduced;

(8) a method of preventing or treating an individual having a ND comprising administering one or more calpain inhibitors or antagonists and at least one other composition used for preventing or treating ND;

(9) a method of determining the presence or absence of a ND in an individual, comprising determining the presence or absence of p25 in a sample obtained from the individual, where the presence of p25 in the sample as compared to a control indicates the presence of the ND, and the absence of p25 as compared to a control indicates the absence of a ND;

(10) a method of determining the presence or absence of a ND in an individual comprisinga) obtaining a sample from an individual to be tested; (b) assessing the levels of p25 and p35 in the sample; and (c) comparing the levels assessed to a standard or control, where an increased level of p25 and a decreased level of p35 indicates relative to a standard indicates the presence of the ND, and a decreased level of p25 and an increased level of p35 indicates relative to a standard indicates the absence of the ND;

(11) a method of diagnosing or aiding in the diagnosis of a ND in an individual comprising: (a) determining the presence, absence or level of p25 in a sample obtained from the individual; and (b) comparing the level of p25 determined with a control or standard, where a presence or increased level of p25 in the sample indicates the presence of the ND, and the absence or decreased level of p25 indicates the absence of a ND;

(12) a method of determining the efficacy of treatment for an individual having a ND, comprising: (a) determining the level of p25 in a sample obtained from the individual; and (b) comparing the level of p25 determined with a control or standard where an increased level of p25 in the sample indicates ineffective treatment and a decreased level of p25 indicates effective treatment;

(13) a method of reducing the extent to which a ND that is associated with neurofibrillatory tangles and accumulation of p25 in the brain occurs in an individual, comprising administering a compound that reduces conversion of p35 to p25 in the brain;

(14) a compound for the prevention or treatment of a ND comprising a compound selected from:

(a) a compound that inhibits the association of p25 with cdk5;

(b) a compound that inhibits deregulation of cdk5 by p25;

(c) a compound that reduces the conversion of p35 to p25;

(d) a compound that reduces the phosphorylation of tau by p25/cdk5 kinase;

(e) a compound that inhibits calpain;

(f) a compound that inhibits a cation; and

(g) a compound that is an agonist of p35;

(15) a nucleic acid construct encoding a compound as in (14).

ACTIVITY - Neuroprotective; Nootropic; Antiparkinsonian; Anticonvulsant.

MECHANISM OF ACTION - p25 Accumulation inhibitors; calpain inhibitors; cation inhibitors; calcium or magnesium inhibitors; p35 agonists; p25-cdk5 association inhibitors; tau phosphorylation inhibitors.

Brain tissues of 8 Alzheimer's disease (AD) cases, 4 age-matched non-neurological cases, and one Huntington's disease case were used in a study. The expression profiles of p35 and cdk5 from human brain tissues were surveyed. While p35 levels remained relatively constant in all samples, a 25kD species, recognizable by anti-p35 antibodies, was

found to be accumulated 20-40-fold that of p35 in all but one AD sample. Cdk5 levels do not vary significantly between normal and AD samples. To verify the identity of the 25kD species, antibodies recognizing various regions of p35 were utilized. The accumulation of this 25kD species in AD samples corresponded to the elevated cdk5 kinase activity in the AD samples as indicated by the cdk5 associated histone H1 kinase activity. It was shown that conversion of p35 to p25 results in deregulation of the cdk5 kinase. The deregulated cdk5 kinase can cause irreversible damage to the cytoskeleton and neuronal death. Based on the accumulation of p25 in AD brains and the cytoskeletal disruption and apoptosis induced by the p25/cdk5 kinase in neurons, p25 production and accumulation in brain may contribute to the pathogenesis of AD. Further studies showed that the calcium dependent protease calpain is responsible for p35 cleavage. Inhibitors to calpain completely inhibit the appearance of p25.

USE - Used to treat or prevent e.g. dementias, NDs associated with stroke, myocardial infarction, ischemia or other oxidative stresses, Alzheimer's disease, Coricobasal degeneration, Dementia pugilistica, Down's syndrome, Frontotemporal dementias and Parkinsonism linked to chromosome 17, Myotonic dystrophy, Niemann-Pick disease, Parkinson-dementia complex of Guam, Pick's disease, postencephalic Parkinsonism, prion disease with tangles, progressive supraneuclar palsy, lower lateral sclerosis, Huntington's disease, subacute sclerosing panencephalistis or **multiple sclerosis** (claimed).

pp; 53 DwgNo 0/4

5/AB/38 (Item 2 from file: 351)
DIALOG(R)File 351:Derwent WPI

008410735
WPI Acc No: 1990-297736/199039
Related WPI Acc No: 1989-270711; 1990-051539; 1993-368986
XRAM Acc No: C90-128636
XRPX Acc No: N90-228849
Testing mammals for susceptibility to inflammatory diseases - by admin. a hypothalamic-pituitary-adrenal axis stimulant and measuring hormone levels
Patent Assignee: US DEPT OF COMMERCE (USDC); NAT INST OF HEALTH (USSH); US SEC OF COMMERCE (USDC); US DEPT HEALTH & HUMAN SERVICE (USSH)
Inventor: CHROUSOS G P; GOLD P W; STERNBERG E M; WILDER R L
Number of Countries: 017 Number of Patents: 008
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
US 7422791	N	19900828	US 89422791	A	19891018	199039	B
WO 9104479	A	19910404				199116	
AU 9065374	A	19910418				199129	
EP 494256	A1	19920715	EP 90915568	A	19900925	199229	
			WO 90US5457	A	19900925		
JP 4504760	W	19920820	JP 90514350	A	19900925	199240	
			WO 90US5457	A	19900925		
US 5209920	A	19930511	US 88277708	A	19881130	199320	
			US 89365735	A	19890614		
			US 89412294	A	19890925		
AU 648274	B	19940421	AU 9065374	A	19900925	199421	
EP 494256	A4	19920812	EP 90915568	A		199523	

Priority Applications (No Type Date): US 89422791 A 19891018; US 88277708 A

19881130; US 89412294 A 19890925; US 89365735 A 19890614
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 9104479	A				
Designated States (National): AU CA JP					
Designated States (Regional): AT BE CH DE DK ES FR GB IT LU NL SE					
EP 494256	A1	E	63	G01N-001/00	Based on patent WO 9104479
Designated States (Regional): AT BE CH DE DK ES FR GB IT LI LU NL SE					
JP 4504760	W		23	G01N-033/74	Based on patent WO 9104479
US 5209920	A		22	G01N-001/00	CIP of application US 88277708 CIP of application US 89365735 CIP of patent US 5006330
AU 648274	B			A61K-037/02	Previous Publ. patent AU 9065374 Based on patent WO 9104479

Abstract (Basic): US 7422791 N

Method for testing mammals for susceptibility to inflammatory diseases comprises administering to a mammal a cpd. (I) which is effective in stimulating the hypothalamic-pituitary-adrenal (HPA) axis and measuring the level of hormones secreted by the pituitary and adrenal glands of the mammal.

More specifically, (I) may be cytokines, cell growth factors, neuroendocrine hormones such as corticotropin releasing hormone (CRH) or arginine vasopressin (AVP), biogenic amines, agonists of biogenic amines, antagonists of biogenic amines, **monoamine oxidase** inhibitors and biogenic amine uptake inhibitors or glucocorticoid receptor antagonists and the level of glucocorticoids or adrenocorticotropic hormone (ACTH) in the blood plasma of the mammal is measured.

USE - Useful as a model in the study of the mammalian autoimmune diseases; also for predicting intensity of response to stress and capacity to mount a sustained adaptive response to stress. Use of therapy through CRH activation during an injury or illness helps prevent the immune-inflammatory response from overshooting and restrains exploratory behaviour to diminish exposure to further danger. Used for testing for susceptibility to inflammatory diseases such as arthritis, uveoretinitis, pneumonitis, encephalomyelitis, myocarditis, thyroiditis, nephritis, **multiple sclerosis** and hepatic granulomatous diseases. The method can also be used as a guide for the treatment with agents that may bypass the HPA defect by stimulating the HPA axis centrally or at multiple levels.

US 7422791 A

Method for testing mammals for susceptibility to inflammatory diseases comprises administering to a mammal a cpd. (I) which is effective in stimulating the hypothalamic-pituitary-adrenal (HPA) axis and measuring the level of hormones secreted by the pituitary and adrenal glands of the mammal.

More specifically, (I) may be cytokines, cell growth factors, neuroendocrine hormones such as corticotropin releasing hormone (CRH) or arginine vasopressin (AVP), biogenic amines, agonists of biogenic amines, antagonists of biogenic amines, **monoamine oxidase** inhibitors and biogenic amine uptake inhibitors or glucocorticoid receptor antagonists and the level of glucocorticoids or adrenocorticotropic hormone (ACTH) in the blood plasma of the mammal is measured.

USE - Useful as a model in the study of the mammalian autoimmune diseases; also for predicting intensity of response to stress and capacity to mount a sustained adaptive response to stress. Use of therapy through CRH activation during an injury or illness helps prevent the immune-inflammatory response from overshooting and restrains exploratory behaviour to diminish exposure to further danger.

Used for testing for susceptibility to inflammatory diseases such as arthritis, uveoretinitis, pneumonitis, encephalomyelitis, myocarditis, thyroiditis, nephritis, **multiple sclerosis** and hepatic granulomatous diseases. The method can also be used as a guide for the treatment with agents that may bypass the HPA defect by stimulating the HPA axis centrally or at multiple levels.

Dwg.0/10

Abstract (Equivalent): US 5209920 A

Testing susceptibility of a mammal to inflammatory disease comprises admin. of a cpd. which stimulates hypothalamic-pituitory-adrenal (HPA) axis and measuring the level of at least one hormone secreted by the pituitary or adrenal glands.

Cpds. is e.g. a cytokine, growth hormone, neuroendocrine hormone, biogenic amine, **monoamine oxidase** inhibitor, etc. Also claimed is a method for treating inflammatory diseases by admin. of the cpd.

USE/ADVANTAGE - For testing susceptibility of mammals to inflammatory diseases, e.g. arthritis, uveoretimitis, pneumonitis, encephalomyelitis, **multiple sclerosis** or hepatic granulomatas.

Dwg.0/8

5/AB/39 (Item 3 from file: 351)

DIALOG(R)File 351:Derwent WPI

008164538

WPI Acc No: 1990-051539/199007

Related WPI Acc No: 1989-270711; 1990-297736; 1993-368986

XRAM Acc No: C90-022306

XRPX Acc No: N90-039601

Testing for susceptibility to inflammatory diseases - by administering cpd. which stimulates hypothalamic-pituitary-adrenal axis and measuring hormone levels

Patent Assignee: US DEPT HEALTH & HUMAN SERVICE (USSH)

Inventor: CHROUSOS G P; GOLD P W; STERNBERG E M; WILDER R L

Number of Countries: 001 Number of Patents: 001

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
US 7365735	N	19891205	US 89365735	A	19890614	199007	B

Priority Applications (No Type Date): US 89365735 A 19890614; US 88277708 A 19881130

Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
US 7365735	N		59		

Abstract (Basic): US 7365735 N

A method for testing mammals for susceptibility to inflammatory diseases comprises administering to a mammal a cpd. (I) which is effective in stimulating the hypothalmic-pituitary-adrenal (HPA) axis and measuring the level of hormones secreted by the pituitary and adrenal glands of the mammal. More specifically (I) may be cytokines, cell growth factors, neuroendocrine hormones such as corticotropin releasing hormone (CRH) or arginine vasopressin (AVP), biogenic amines, agonists of biogenic amines, antagonists of biogenic amines, **monoamine oxidase** inhibitors and biogenic amine uptake inhibitors or glucocorticoid receptor antagonists and the hormones measured may be e.g. glucocorticoids or adrenocorticotropic hormone (ACTH) in the blood plasma.

USE/ADVANTAGE - After administration of (I) the hormones are secreted in lower levels in individuals having an inflammatory disease or susceptibility to an inflammatory disease. m for testing for susceptibility to inflammat e.g. arthritis, uveoretinitis, myocarditis, **multiple sclerosis** and hepatic granulomatous diseases. It may also be used as a guide for the treatment of arthritis with agents that may bypass the HPA defect by stimulating the HPA axis centrally or at multiple levels. It may also provide a guide for detn. of dosage and timing schedule of replacement steroids or other HPA axis hormones such as CRH or ACTH.

Dwg.0/8

US 7365735 A

A method for testing mammals for susceptibility to inflammatory diseases comprises administering to a mammal a cpd. (I) which is effective in stimulating the hypothalamic-pituitary-adrenal (HPA) axis and measuring the level of hormones secreted by the pituitary and adrenal glands of the mammal. More specifically (I) may be cytokines, cell growth factors, neuroendocrine hormones such as corticotropin releasing hormone (CRH) or arginine vasopressin (AVP), biogenic amines, agonists of biogenic amines, antagonists of biogenic amines, **monoamine oxidase** inhibitors and biogenic amine uptake inhibitors or glucocorticoid receptor antagonists and the hormones measured may be e.g. glucocorticoids or adrenocorticotropic hormone (ACTH) in the blood plasma.

USE/ADVANTAGE - After administration of (I) the hormones are secreted in lower levels in individuals having an inflammatory disease or susceptibility to an inflammatory disease. m for testing for susceptibility to inflammat e.g. arthritis, uveoretinitis, myocarditis, **multiple sclerosis** and hepatic granulomatous diseases. It may also be used as a guide for the treatment of arthritis with agents that may bypass the HPA defect by stimulating the HPA axis centrally or at multiple levels. It may also provide a guide for detn. of dosage and timing schedule of replacement steroids or other HPA axis hormones such as CRH or ACTH.

5/AB/40 (Item 4 from file: 351)
DIALOG(R)File 351:Derwent WPI

008005599
WPI Acc No: 1989-270711/198937
Related WPI Acc No: 1990-051539; 1990-297736; 1993-368986
XRAM Acc No: C89-119881
Testing for susceptibility to inflammatory diseases - by administering cpd. which stimulates hypothalamic-pituitary-adrenal axis and measuring hormone levels
Patent Assignee: US DEPT HEALTH & HUMAN SERVICE (USSH); US SEC OF COMMERCE (USDC)
Inventor: CHROUSOS G P; GOLD P W; STERNBERG E M; WILDER R L
Number of Countries: 016 Number of Patents: 008
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
US 7277708	N	19890711	US 88277708	A	19881130	198937	B
WO 9006112	A	19900614				199027	
CA 2004133	A	19900531				199033	
AU 9048039	A	19900626				199038	
US 5006330	A	19910409	US 88277708	A	19881130	199117	
EP 446282	A	19910918	EP 90900690	A	19891130	199138	
JP 3503803	W	19910822	JP 90501334	A	19891130	199140	

EP 446282 A4 19930421 EP 90900690 A 199526

Priority Applications (No Type Date): US 88277708 A 19881130; US 89365735 A 19890614

Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
US 7277708	N		52		
WO 9006112	A				
Designated States (National): AU JP					
Designated States (Regional): AT BE CH DE ES FR GB IT LU NL SE					
EP 446282	A				
Designated States (Regional): AT BE CH DE ES FR GB IT LI LU NL SE					

Abstract (Basic): US 7277708 N

A method for testing mammals for susceptibility to inflammatory diseases comprises administering to a mammal a cpd. (I) which is effective in stimulating the hypothalamic-pituitary-adrenal (HPA) axis and measuring the level of hormones secreted by the pituitary and adrenal glands of the mammal.

More specifically, (I) may be cytokines, cell growth factors, corticotropin releasing hormone (CRH); biogenic amines, agonists of biogenic amines, antagonists of biogenic amines, analogues of biogenic amines, **monoamine oxidase** inhibitors and biogenic amine uptake inhibitors or glucocorticoid receptor antagonists and the level of glucocorticoids (GCs) or adrenocorticotropic hormone (ACTH) in the blood plasma of the mammal.

USE - If the hormone levels secreted are lower than normal then the test is postiive for susceptibility for inflammatory diseases including arthritis, uveoretinitis, pneumonitis, encephalomyelitis, **multiple sclerosis** and hepatic granulomatous diseases. It may also be useful as a guide for the treatment of inflammatory diseases with agents that may bypass the HPA defect by stimulating the HPA axis centrally or at multiple levels. It may also provide a guide for determn. of dosage and timing schedule of replacement steroids or other HPA axis hormones such as CRH or ACTH.

Dwg.0/8

US 7277708 A

A method for testing mammals for susceptibility to inflammatory diseases comprises administering to a mammal a cpd. (I) which is effective in stimulating the hypothalamic-pituitary-adrenal (HPA) axis and measuring the level of hormones secreted by the pituitary and adrenal glands of the mammal.

More specifically, (I) may be cytokines, cell growth factors, corticotropin releasing hormone (CRH); biogenic amines, agonists of biogenic amines, antagonists of biogenic amines, analogues of biogenic amines, **monoamine oxidase** inhibitors and biogenic amine uptake inhibitors or glucocorticoid receptor antagonists and the level of glucocorticoids (GCs) or adrenocorticotropic hormone (ACTH) in the blood plasma of the mammal.

USE - If the hormone levels secreted are lower than normal then the test is positive for susceptibility for inflammatory diseases including arthritis, uveoretinitis, pneumonitis, encephalomyelitis, **multiple sclerosis** and hepatic granulomatous diseases. It may also be useful as a guide for the treatment of inflammatory diseases with agents that may bypass the HPA defect by stimulating the HPA axis centrally or at multiple levels. It may also provide a guide for determn. of dosage and timing schedule of replacement steroids or other HPA axis hormones such as CRH or ACTH.

Abstract (Equivalent): US 5006330 A

The susceptibility of a mammal to an inflammatory disease is

treated by A) administering to the mammal a sufficient amount of interleukin-1 to stimulate the hypothalmicitpuitary-adrenal axis and B) measuring the level of hormone(s) secreted by the pituitary or adrenal glands in the blood plasma of the mammal.

The hormones are pref. the glucocorticoid or adrenocorticotropic hormones. The disease can be arthritis, uveoretinitis, pneumonitis, encephalomyelitis, **multiple sclerosis** or hepatic granulomatas. The mammal is esp. human and the disease is arthritis.

ADVANTAGE - An effective test. (20pp

5/AB/41 (Item 5 from file: 351)
DIALOG(R)File 351:Derwent WPI

004184942
WPI Acc No: 1985-011822/198502
Related WPI Acc No: 1983-801098
XRAM Acc No: C85-004998
XRPX Acc No: N85-008525
Treating arthritis with isocarboxazid - to inhibit biosynthesis of prostaglandin E2
Patent Assignee: LIEB J (LIEB-I)
Inventor: LIEB J
Number of Countries: 001 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
US 4490385	A	19841225	US 83539306	A	19831005	198502	B

Priority Applications (No Type Date): US 83539306 A 19831005; US 81319651 A 19811109
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
US 4490385	A		4		

Abstract (Basic): US 4490385 A

Arthritis is treated by administration of isocarboxazid (I) as **monoamine oxidase** inhibitor. The pref. oral dose is 5-60 mg/day.

USE - (I), and other **MAO** inhibitors, are already known for treatment of depression and are now found to inhibit prostaglandin, esp. PGE 2, biosynthesis. They are thus useful for treating a wide variety of inflammatory and autoimmune conditions associated with excessive PGE2 levels, e.g. arthritis, **multiple sclerosis**, diabetes, lupus arythematosus and infertility.

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5/AB/42 (Item 6 from file: 351)
DIALOG(R)File 351:Derwent WPI

003804857
WPI Acc No: 1983-801098/198343
XRAM Acc No: C83-104680
Arthritis treatment with **monoamine oxidase** inhibitors - i.e. mebanazine or uranyl cypromine
Patent Assignee: LIEB J (LIEB-I)
Inventor: LIEB J
Number of Countries: 001 Number of Patents: 001

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
US 4409243	A	19831011				198343 B

Priority Applications (No Type Date): US 81319651 A 19811109; US 83539306 A 19831005

Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
US 4409243	A		4		

Abstract (Basic): US 4409243 A

Arthritis treatment comprises admin. of a **monoamine oxidase** inhibitor which is metanazine (I) or tranylcupromine (II). Oral doses are e.g. 5-50 mg/day (I) and up to 60 mg/day (II).

In an example, a manic-depressive female patient on Li therapy (900 mg/day) was diagnosed to be suffering from rheumatoid arthritis in the knees and fingers. When receiving (II) at 40 mg/day for treatment of the depressive phase it was noticed that the arthritic pain had disappeared.

Monoamine oxidase inhibitors (MAOI) are used for ameliorating immunity and inflammatory disorders characterised by excessive PGE2 biosynthesis, e.g. rheumatoid and allergic arthritis; certain virus induced conditions, e.g. Guillain Barre syndrome, infectious mononucleosis, other viral lymphadenopathines and infectious with herpes virus; demyelinating diseases, e.g. **multiple sclerosis**; haematological disorders, e.g. hemoltyic anaemia and thrombocytopenia, endocrinological disorders, e.g. diabetes mellitus, Addisons disease; collagen disorders, e.g. systemic lupus erythematosus; and reproductive disorders, e.g. amenorrhoea, infertility, recurrent abortions and eclampsia.

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